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The Mechanism of Cerium(IV) Oxidation of Glucose and Cellulose

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THE MECHANISM OF CERIUM(IV) OXIDATION OF GLUCOSE AND CELLULOSE

A thesis submitted by

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SUMMARY

The mechanisms of cerium(IV) oxidations of model compounds for cellulose were studied in aqueous 1.0M perchloric acid at 20.0°C. Definite evidence for the participation of intermediate complexes was obtained by kinetic methods for reactions of D-glucose, Schardinger β-dextrin (anhydro-D-glucose), 1,5-anhydro-D-glucitol, and methyl β-D-glucopyranoside. Corroborating evidence for the participation of intermediate complexes was obtained using an independent spectrometric technique for reactions of Schardinger β-dextrin, 1,5-anhydro-D-glucitol, and methyl β-D-glucopyranoside. For all of these 1,2-glycol-containing compounds the magnitudes of the equilibrium constants for complex formation are considerably higher than the values found for monohydric alcohols. The increase in complex stability exhibited by these compounds indicates that the intermediate complexes are chelates.

The effect of O-methyl substitution on the reactivity of vicinal diol groups with cerium(IV) was studied. Oxidation of methyl β-D-glucopyranoside, which contains α-glycol sites and the C_1-O-methyl-C_2-O-hydrogen site, takes place at an α-glycol site. However, for 2-O-methyl-D-glucose, which has a glycol site at C_3-C_4, a monomethylated-diol site at C_2-C_3, and a monomethylated diol involving the C_1 reducing carbon, the reaction takes place at the reducing group resulting in cleavage of the C_1-C_2 bond. In fact, 2-O-methyl-D-glucose is oxidized slightly faster than D-glucose and both yield the same product, D-arabinose. From these results it is concluded that the hydroxyl of the reducing carbon is the most reactive hydroxyl in aldoses and that the O-methyl group facilitates the cleavage of the bond between its carbon and an adjacent carbon, when the hydroxyl group on the adjacent carbon is coordinated with attacking cerium(IV) species.

The similarity of oxidation rates of α-glycols and their monomethyl ethers is explained by considering the stability and reactivity of the intermediate complexes involved. For α-glycols which form stable chelate complexes the rate of complex disproportionation is low, while the 2-methoxyalcohols form less stable, probably acyclic, complexes which disproportionate very rapidly.

The proposed mechanism of D-glucose oxidation involves a chelate complex between cerium(IV) and the C_1-C_2 hydroxyls of glucose which disproportionates by homolytic cleavage of the C_1-C_2 bond forming a free radical on either C_1 or C_2. The free radical is rapidly oxidized by a second mole of cerium(IV). This mechanism is consistent with the kinetic behavior of the system and the primary products of the reaction, D-arabinose and formic acid.

The proposed mechanism of Schardinger β-dextrin (model for anhydro-D-glucose[1] units) oxidation by cerium(IV) involves the formation of a complex between the oxidant and the C_2-C_3 diol. The complex disproportionates homolytically, cleaving the C_2-C_3 bond forming an aldehyde function and a free radical on the respective carbon atoms. The free radical is further oxidized by a second mole of cerium(IV) yielding a second aldehyde group. Hydrolysis of oxidized anhydro-D-glucose models (Schardinger β-dextrin and cellulose) yields erythrose and glyoxal as required by the proposed mechanism.

The results of these studies are related to the oxidative phase of initiating vinyl polymerization onto cellulose by cerium(IV). The relative reactivities of the reducing end group versus the anhydro-D-glucose repeating unit and nonreducing end-group were estimated. The reducing group model was 360 times more reactive than the model for the anhydro-D-glucose unit and 240 times more

[1] The term anhydro-D-glucose is used throughout this paper to signify the monomeric repeating units found in 1-4 linked glucan polymers such as amylose and cellulose.

reactive than the model for the nonreducing end-group. However, considering the relatively low concentration of end-groups in most cellulose samples it appears that the major point of graft initiation is either the C_2 or C_3 carbon atoms of anhydro-D-glucose units. As the degree of polymerization of a cellulose is reduced the amount of oxidant consumed by the reactive end-group should increase so that in the presence of vinyl monomers the resulting product should be a cellulose-vinyl block copolymer.

INTRODUCTION

The possibility of modifying cellulosic materials by graft copolymerization with vinyl monomers has directed research effort to various methods of generating free radicals. The ceric ion-alcohol redox system, suggested by Mino and Kaizerman (1), has received much attention. The mechanism of free radical formation is believed (1-6) to involve the formation of a complex between ceric ion and cellulosic hydroxyl groups. The complex then disproportionates unimolecularly forming a free radical (6) on the cellulose backbone. The free radical initiates polymerization when vinyl monomers, M, are present. The mechanism can be summarized as follows (5):

$$Ce(IV) + ROH \rightleftarrows Complex \rightarrow Ce(III) + H^{+} + \dot{R}OH$$

$$\dot{R}OH + M \rightarrow R(OH)M\cdot$$

$$\dot{R}(OH)M + nM \rightarrow R(OH)M_{n+1}$$

The polymerization is terminated by cerium(IV) oxidation of the free radical (2,7).

The kinetics of polymerization reactions in ceric ion-alcohol systems using pinacol (2), ethylene glycol (3), and clinical dextran (4) all support the proposed mechanism. Electron spin resonance studies (6) have demonstrated the existence of free radicals in purified cotton cellulose and microcrystalline cellulose reacted with cerium(IV). The formation of carbon-carbon bonds between the substrate and the vinyl polymer has been established. Iwakura, et al. (8) have demonstrated that, in ceric ion-ethanol initiated styrene polymerization, the resulting polystyrene contains hydroxyl groups. The presence of hydroxyl groups confirms the existence of the carbon radical, $\dot{R}OH$, rather than the alkoxy

radical, RO·, as the initiating species. Work with polymeric systems also indicate primary bonds between substrate and grafted polymer (9,10).

Much evidence concerning the mechanism of the reactions of alcohols and glycols has been obtained from studies of simple organic compounds. Duke and coworkers (11,12) devised a method which quantitatively demonstrated the presence of cerium(IV)-alcohol complexes as intermediates in oxidation of 2,3-butanediol. The formation of intermediate complexes in oxidations by cerium(IV) has been repeatedly shown by subsequent workers (5,13-16).

The details of the cerium(IV)-cellulose reaction, in which the free radical is generated, have not been elucidated. Since cerium(IV) is known to oxidize simple alcohols, it is expected (5,17,18) that free radicals are generated at C_2, C_3, or C_6 of anhydro-D-glucose units. Terasaki and Matsuki (19) studied the oxidation of cellulose by cerium(IV) and found a fast initial reaction. They suggested that the rapid initial reaction corresponded to oxidation of reducing C_1 hydroxyls. Wallace and Young (4) attributed the rapid initial rate of acrylamide polymerization, initiated by a cerium(IV)-dextran system, to the rapid reaction of cerium(IV) with cis-glycol groups on the ends of dextran chains. However, there is evidence that the rapid initial polymerization is related to reaction of cerium(IV) with hydroxyl groups in the amorphous zones of cellulose (20). Neimo and Sihtola (21) suggested that the properties of cellulose-acrylamide copolymers are best explained by a block copolymer structure in which polymerization is initiated at the hemiacetal group of cellulose. Iwakura, et al. (8) in a study of model compounds for cellulose postulated that since glucose was more efficient as an initiator of vinyl polymerizations than trans-1,2-cyclohexanediol, grafting may occur selectively at hemiacetal end groups. It was concluded (8), however, that the low concentration of end groups with respect to the concentration of

anhydro-D-glucose units in cellulose makes some reaction at other reactive centers likely.

The results of two studies suggest the possibility of preferential attack by cerium(IV) on the C_2-C_3 diol of anhydro-D-glucose units. In a study of initiation of vinyl polymerization by methyl celluloses of varying degrees of substitution, it was found that grafting did not occur in methyl celluloses containing no α-glycols, but grafting was rapid in methyl celluloses which contained α-glycol groups (20). Also, cerium(IV) oxidations of polyvinyl alcohol occur preferentially at 1,2-glycol groups rather than at normal 1,3-glycol units (22).

The apparent importance of α-glycol groups in reactions with cerium(IV), which suggests the importance of the C_2-C_3 glycol of anhydro-D-glucose, is believed to be related to the possibility of chelate formation. The existence of intermediate cerium(IV)-α-glycol complexes has been demonstrated, but the nature of these complexes is not understood. Duke (23) assumed that when a reductant is 1,2-oxygenated it is necessarily bidentate and forms a chelate complex. Offner (24, 25) compared the equilibrium constants for complex formation of diethylene glycol and several monohydric alcohols and concluded that the increased stability of the cerium(IV)-diethylene glycol complex was probably due to the formation of a five-membered chelated ring structure (24,25). Littler and Waters (15) found that ethylene glycol and 2-methoxyethanol were both oxidized via complex intermediates and at approximately the same rate. They assumed that chelate complex formation with 2-methoxyethanol was impossible and by analogy of the overall rates concluded that oxidations of 1,2-diols proceed by an acyclic mechanism. Hintz (5) pointed out, however, that the substrate concentration range used by Littler and Waters was too high to permit the determination of complex formation constants and that

conclusions based solely on relative rates were unreliable. Hintz and Johnson (26) studied the cerium(IV) oxidations of cis- and trans-cyclohexanediols and concluded that chelate complexes were involved in the equilibrium step. Comparison of the relative magnitude of complex formation constants for oxidations of trans-1,2-cyclohexanediol and trans-2-methoxycyclohexanol showed that the substitution of a methyl group for a hydroxyl hydrogen reduced complex stability, apparently preventing chelation. However, the overall rates of oxidation for trans-1,2-cyclohexanediol and its monomethyl ether were practically identical, as Littler and Waters found for ethylene glycol and 2-methoxyethanol. The much larger equilibrium constants for complex formation found for the diols suggests that the oxidation of 1,2-diols by cerium(IV) occurs by a chelate intermediate mechanism.

The purpose of this research was to study the cerium(IV) oxidations of selected carbohydrates and carbohydrate derivatives, which were assumed to be valid models for the anhydro-D-glucose units of cellulose. From detailed information concerning the kinetics and products of oxidation reactions of model systems, it was postulated that the mechanism and most probable position of free radical generation on cellulose could be assigned. The importance of the hemiacetal end-group and the nature of its cerium(IV) complex were determined by studies of glucose and glucose derivatives in which the substituents on C_1 and C_2 were changed.

The following sections review some of the literature pertaining to the nature of cerium(IV) as an oxidant and to oxidations of alcohols and glycols.

PROPERTIES OF CERIUM(IV) IN ACID SOLUTIONS

The normal oxidation states of cerium salts are three and four (27); therefore, monomeric cerium will be a one-electron oxidant. The oxidation potential of the cerium(IV)-cerium(III) couple depends upon the acid anion and the acid concentration as shown in Table I. According to the assumption of a simple acid solution of

cerium(IV) and cerium(III) ions the concentration and identity of the mineral acid should not affect the oxidation potential (29). However, it is found that increasing acid concentration increases oxidation potential in perchloric acid and decreases the potential in nitric and sulfuric acids. Furthermore, changing from perchloric to nitric or sulfuric acids, at a given concentration, reduces the oxidation potential. These results indicate the existence of cerium(IV) complexes with certain anions. The oxidation potential decreases as the ability of the anion to form stable complexes increases. Sulfate ion forms stable complexes with cerium(IV) (30), where perchlorate ion probably does not complex at all. The increase in potential with increasing perchloric acid concentration has been attributed to variation of ionic strength and cerium(IV) hydrolysis equilibria (31). The reverse behavior observed with nitric and sulfuric acids indicates that with these anions increased complexing more than compensates for effects of decreasing hydrolysis due to increased acidity (5).

TABLE I

CERIUM(IV)-CERIUM(III) HALF-CELL POTENTIALS[a]

Acid Normality	$HClO_4$	HNO_3	H_2SO_4	HCl
1	-1.70	-1.61	-1.44	-1.28
2	-1.71	-1.62	-1.44	--
4	-1.75	-1.61	-1.43	--
6	-1.82	-1.56	--	--
8	-1.87	--	-1.42	--

[a]Data from reference (28).

The nature of cerium(IV) species in acid solution has been studied extensively. The evidence for complex formation is based on determinations of the effect of concentration variables on the cerium(IV)-cerium(III) half-cell potentials and on absorption spectra of cerium(IV) solutions.

Cerium(IV), in aqueous perchloric acid, has been shown to exist as a mixture of Ce^{4+}, $CeOH^{3+}$, $Ce(OH)_2^{2+}$, and a dimer, probably $(Ce\text{-}O\text{-}Ce)^{6+}$ (32). There is much evidence supporting the existence of hydrolyzed and dimeric species (31-37). Hardwick and Robertson (32) studied the spectra of cerium(IV) solutions and found that the data were explained by the hydrolysis reaction

$$Ce^{4+} + H_2O \rightleftarrows CeOH^{3+} + H^+.$$

The equilibrium constant for the above reaction was large; the presence of the hydrolyzed species, $CeOH^{3+}$, was favored. Other workers (24,31,37) found that the controlling equilibrium is best represented by the reaction,

$$CeOH^{3+} + H_2O \rightleftarrows Ce(OH)_2^{2+} + H^+,$$

for which the equilibrium constant is small. Therefore, the results of all authors agree and indicate that, due to the magnitude of the equilibrium constants involved, the most important species in aqueous solutions of cerium(IV) is $CeOH^{3+}$. The formation of dimeric cerium(IV) species is negligible at low cerium(IV) concentrations (32,36).

Hardwick and Robertson (30) spectrophotometrically determined the equilibrium constants for the formation of cerium(IV)-sulfate complexes in 1.0M sulfuric acid according to the following equilibria at 25°C.

$$Ce^{4+} + HSO_4^- \overset{K_1}{\rightleftarrows} Ce(SO_4)^{2+} + H^+ \quad K_1 = 3500$$

$$Ce(SO_4)^{2+} + HSO_4^- \overset{K_2}{\rightleftharpoons} Ce(SO_4)_2 + H^+ \quad K_2 = 200$$

$$Ce(SO_4)_2 + HSO_4^- \overset{K_3}{\rightleftharpoons} Ce(SO_4)_3^{2-} + H^+ \quad K_3 = 20$$

Hardwick and Robertson (30) also showed the presence of the anionic species, $Ce(SO_4)_3^{2-}$, by migration studies and the absence of hydrolyzed species, as suggested earlier (38), since the absorbance of cerium(IV) solutions was unaffected by changes in acid concentration at a constant ratio of hydrogen ion to bisulfate ion.

The ability of cerium(IV) to form inorganic complexes greatly affects the oxidations of organic compounds. The general reduction of organic oxidation rates as the ability of the acid anion to form stable cerium(IV) complexes increases has been used as a tool in the study of extremely fast reactions. Hintz (5,26) found that cis-1,2-cyclohexanediol was oxidized 3000 times faster in 1.0M perchloric than in mixed 0.25M sulfuric and 0.75M perchloric acids. Also the rates of cis- and trans-1,2-cyclopentanediols, which were too great to be measured in 1.0M perchloric acid, were easily determined in mixed 0.25M sulfuric and 0.75M perchloric acids. The same effect was observed in this work; glucose was oxidized 840 times faster in 1.0M perchloric acid than in mixed 0.25M sulfuric and 0.75M perchloric acids. More important to studies dealing with mechanism of organic oxidations, the complexing of the acid anion may affect the ability of cerium(IV) to complex with organic compounds. Offner (24) found consistently lower complex formation constants for cerium(IV)-alcohol complexes in nitric acid than in perchloric acid. Muhammad and Rao (39,40) found that methanol is oxidized via an intermediate complex in perchloric acid, but could not detect complex formation in sulfuric acid media. Hintz (5) also found that although cis- and trans-1,2-cyclohexanediols are oxidized through complex intermediates in perchloric acid, no evidence for complexing was obtained for the oxidations of cis- and trans-1,2,-cyclopentanediols in sulfate-containing systems. Generally, it has been found that

complex formation takes place readily in perchloric acid and is easily detectable, whereas for reactions of the same compounds in sulfuric or nitric acids complexing with organic ligands is a competing process and complex detection is difficult.

ORGANIC OXIDATIONS AND OXIDANT-REDUCTANT COMPLEXES

The recent reviews of Hintz (5) and Richardson (41) discuss literature pertinent to the importance of coordination complexes in mechanisms of cerium(IV) and other oxidant reactions. However, a brief discussion is included in this section to provide necessary information concerning these types of reactions.

Cerium(IV) is a one-electron oxidant; therefore, oxidations of alcohols or diols, requiring the removal of two electrons, demand an overall reaction stoichiometry of two moles cerium(IV) per mole alcohol reacted. The general oxidation mechanism for reactions in acid media postulated by Levitt (42) can be modified to include one-electron oxidants. The proposed mechanism for cerium(IV) oxidations is: (1) the oxidant and reductant interact to form a complex, which may be the result of an equilibrium step or simply a direct formation of the transition state, which is positively charged; (2) the coordination complex disproportionates homolytically in the rate-controlling step in which the oxidant captures one electron, the reductant becomes a free radical, and a proton is displaced; (3) the free radical is then rapidly oxidized by a second cerium(IV) species to form the reaction product and displacing a second proton.

The generation of free radicals as intermediates in cerium(IV) oxidations has been quantitatively demonstrated by polymerization and electron spin resonance studies. Arthur and coworkers (6) showed by electron spin resonance that free radicals were present in cerium(IV) treated cellulose. Evidence for free radical formation and for grafting with organic compounds was obtained by Mino, et al. (2)

who showed that, in the ceric sulfate oxidation of pinacol, the ratio of cerium(IV) consumed to acetone formed changed from one to two when acrylamide was added to the system.

Unlike periodate and lead tetraacetate which are specific oxidants for unhindered 1,2-glycols, cerium(IV) is a powerful oxidant capable of oxidizing alcohols, glycols, aldehydes, ketones, acids, and unsaturated hydrocarbons. The fact that cerium(IV) is a general oxidant, like permanganate, presents the problem of possible secondary oxidation of initial reaction products.

Some reactions of alcohols and α-glycols which have been studied are given in Table II, which shows observed products and stoichiometry. In all cases the predicted stoichiometry, two moles cerium(IV) consumed per mole alcohol oxidized, is observed and the products are carbonyl compounds.

THEORY OF OXIDATIONS INVOLVING INTERMEDIATE COMPLEXES

With the exception of one reported study (44), cerium(IV) oxidations of organic substrates are generally believed to involve direct transfer of a single electron. It seems reasonable that the reaction mechanism will include an interaction between the cerium(IV) and the organic substrate. Two types of mechanisms can be distinguished depending on the nature of this interaction. In the first mechanism a stable coordination complex is formed between the cerium(IV) and the organic substrate, R, in a rapid preliminary equilibrium step. The intermediate complex then disproportionates, unimolecularly, in the rate-determining step forming cerium(III) and a free radical R·

$$Ce(IV) + R \overset{K}{\rightleftharpoons} Complex \xrightarrow[slow]{k} Ce(III) + R\cdot + H^{+} \qquad (1).$$

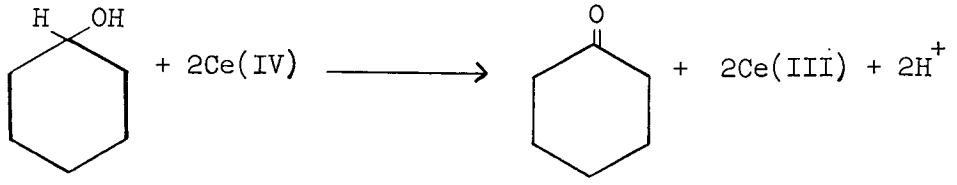
TABLE II

REACTIONS OF ALCOHOLS WITH CERIUM(IV)

1. Methanol (39,40)

$$CH_3OH + 2Ce(IV) \longrightarrow H_2C = O + 2Ce(III) + 2H^+$$

2. Cyclohexanol (5,43)



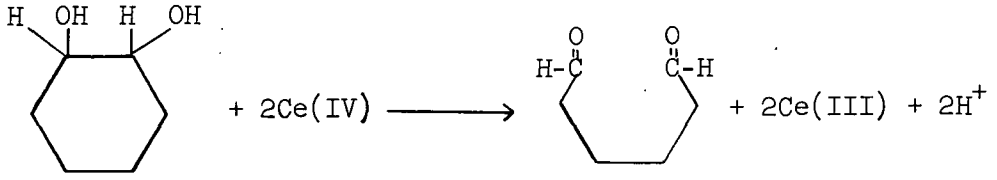
3. 2,3-Butanediol (11,12)

$$CH_3\text{-}\underset{OH}{CH}\text{-}\underset{OH}{CH}\text{-}CH_3 + 2Ce(IV) \longrightarrow 2CH_3\text{-}\overset{O}{\overset{\|}{C}}\text{-}H + 2Ce(III) + 2H^+$$

4. Pinacol (2)

$$(CH_3)_2\text{-}\underset{HO}{\overset{OH}{C}}\text{-}\overset{OH}{\underset{O}{C}}\text{-}(CH_3)_2 + 2Ce(IV) \longrightarrow 2(CH_3)_2\text{-}C = O + 2Ce(III) + 2H^+$$

5. 1,2-Cyclohexanediol (5,18)



The free radical is rapidly oxidized by a second mole of cerium(IV):

$$Ce(IV) + R\cdot \xrightarrow{fast} Ce(III) + Product + H^+ \qquad (2).$$

The second mechanism assumes that the substrate is oxidized directly by cerium(IV). In this case the interaction takes place in the transition state:

$$Ce(IV) + R \rightarrow [Ce(IV) \text{ --- } R] \longrightarrow Ce(III) + R\cdot + H^+ \qquad (3).$$

As in the first mechanism, the free radical is rapidly oxidized by a second mole of cerium(IV).

The participation of intermediate complexes in the reaction mechanism can be evaluated from kinetic data. Duke (23) originally derived the general theory for oxidations involving intermediate complexes and was the first to apply it to cerium(IV) oxidations (11,12). It is assumed: (1) that the stoichiometry of the complex [Equation (1)] requires one oxidant and one substrate molecule; (2) that coordination equilibrium is rapidly established and that equilibrium is maintained despite the unidirectional disproportionation of the complex; and (3) the free radical formed is rapidly oxidized by a second mole of cerium(IV). Then the rate expression corresponding to this mechanism is

$$-d[Ce(IV)_T]/dt = \left[kK[R]/(1 + K[R])\right] [Ce(IV)_T] \qquad (4)$$

where $[Ce(IV)_T]$ is the total cerium(IV) concentration (5,24). In the presence of excess substrate the rate expression becomes psuedo-first-order with respect to total cerium(IV) concentration

$$-d[Ce(IV)_T]/dt = k' [Ce(IV)_T] \qquad (5)$$

where

$$k' = kK[R]/(1 + K[R]) \qquad (6)$$

The equilibrium constant for complex formation, $\underline{K}$, and the rate constant for complex disproportionation, $\underline{k}$, can be experimentally evaluated by determining the pseudo-first-order rate constant, $\underline{k}'$, at a number of substrate concentrations. Then, since

$$1/k' = 1/k + 1/kK[R] \tag{7}$$

$\underline{K}$ and $\underline{k}$ can be calculated from the slope and intercept of a plot of $1/\underline{k}'$ versus $1/[\underline{R}]$. This plot is generally referred to as a reciprocal plot. The finding of a linear reciprocal plot with a significant intercept provides definite evidence for participation of intermediate complexes in the reaction mechanism.

Examination of Equation (4) shows that if the equilibrium constant, $\underline{K}$, is small then the term $\underline{K}[\underline{R}]$ can be negligible with respect to one and the rate expression becomes second order,

$$-d\ [Ce(IV)_T]/dt = k_{II}[R]\ [Ce(IV)] \tag{8}$$

where

$$k_{II} = kK \tag{9}.$$

Therefore, the finding of second-order kinetics does not exclude the possibility of complex formation in the reaction mechanism. Second-order behavior is an ambiguous case in which it cannot be ascertained whether (1) the equilibrium constant, $\underline{K}$, is small; (2) complex formation is the rate-determining step; or (3) the reaction actually involves a direct bimolecular oxidation mechanism. It is impossible to evaluate the participation of complex formation in the mechanism if second-order kinetics are obtained.

From the above discussion it is apparent that both the complex-intermediate and the direct bimolecular reactions predict first-order behavior with respect to cerium(IV). In agreement with this prediction, cerium(IV) oxidations always give first-order kinetics. However, consideration of the predicted rate expressions,

Equations (5) and (8), shows that the dependence of the rate on the substrate concentration predicted by the two mechanisms is quite different. The difference in the dependence on substrate concentration provides a method for distinguishing between the mechanisms. In either case, when the substrate is present in large excess the reaction becomes pseudo-first-order with respect to cerium(IV). The pseudo-first-order rate constant is a function of substrate concentration in which the nature of the relationship depends on the mechanism of oxidation. It can be seen from Equation (6) that a plot of $\underline{k}'$ versus [R] will be nonlinear, concave downward and pass through the origin, if the intermediate complex mechanism is operative. The direct oxidation mechanism, Equation (8), predicts a linear relationship between $\underline{k}'$ and [R] where $\underline{k}' = \underline{k}_{II}[R]$. As previously discussed, evidence for second-order behavior cannot be rigorously interpreted.

The observation that cerium(IV) solutions in perchloric and nitric acid become a deeper red when ethanol is added has long been recognized as a test for the alcohol functional group (45,46). The color change is due to complex formation and spectrometric methods have been devised to quantitatively determine the equilibrium constant for complex formation, K. Ardon (16) developed a method based on the change of absorbance of cerium(IV) solutions at a number of substrate concentrations. Values of complex formation constants determined by Ardon's technique have been obtained which agree well with kinetically determined values for cerium(IV) oxidations of ethanol (16), methanol (40), glycerol (47), methyl ethyl ketone and acetone (48), cis- and trans-1,2-cyclohexanediols and trans-2-methoxycyclohexanol (5,26). Offner (24) developed a different spectrometric technique for determining complex formation constants. As in the kinetic methods, the spectrometric techniques cannot accurately determine small values of the equilibrium constant.

Ardon's technique relates the color change due to complex formation to the complex formation constant, K, for reactions proceeding through a 1:1 complex:

$$Ce(IV) + R \underset{}{\overset{K}{\rightleftharpoons}} C \xrightarrow{k} \text{Products}.$$

If the substrate, R, is a nonabsorbing species and the oxidant, Ce(IV), and the complex, C, are the only absorbing species, then the absorbance, A, is given by the equation

$$A = \varepsilon_c [C] + \varepsilon_a ([T] - [C]) \tag{10}$$

where

ε_c = molar absorptivity of the complex

ε_a = molar absorptivity of the oxidant

[C] = concentration of complex

[T] = total concentration of oxidant.

Since the total concentration of oxidant, [T], can be expressed

$$[T] = [C] + [Ce(IV)] \tag{11}$$

and

$$K = [C]/[Ce(IV)]\,[R] \tag{12}$$

then

$$[C] = K\,[T]\,[R]/(1 + K\,[R]) \tag{13}.$$

Substituting Equation (13) into Equation (10)

$$A = \Delta\epsilon \left[K[R]/(1 + K[R])\right]\,[T] + \epsilon_a[T] \tag{14}$$

where $\Delta\epsilon = \epsilon_c - \epsilon_a$. Defining, $A_b = \epsilon_a\,[T]$, as the absorbance of the oxidant solution in the absence of the substrate, gives the expression

$$A - A_b = \Delta\epsilon \left[K[R]/(1 + K[R])\right]\,[T] \tag{15}$$

which at zero time becomes

$$A_o - A_b = \Delta\epsilon\left[K[R]/(1 + K[R])\right] [T]_o \qquad (16)$$

or

$$1/(A_o - A_b) = 1/\Delta\epsilon[T]_o + 1/\Delta\epsilon [T]_o K [R] \qquad (17)$$

The equilibrium constant, $\underline{K}$, can be calculated from the slope and intercept of a plot of $1/(\underline{A_o} - \underline{A_b})$ versus $1/[\underline{R}]$ where $\underline{K}$ = intercept/slope.

Studies of cerium(IV) oxidations have been made in perchloric, nitric, and sulfuric acids. In considering the results of kinetic studies the complexing ability of the acid anion with cerium(IV) must be considered. Thus, cerium(IV) oxidations in sulfuric acid, where the sulfate anion forms a stable complex with cerium(IV), are generally second-order. However, recent studies of cerium(IV) oxidation of arabinose (49) and oxalate (50) in sulfuric acid report evidence for complex formation. In perchloric acid, which does not complex with cerium(IV), all oxidations of oxygenated organic compounds, with the exception of formaldehyde (51), have provided evidence for complex formation. It appears that detection of cerium(IV)-organic complexes is dependent on the stability of the cerium(IV)-inorganic species present. Increasing the stability of the cerium(IV)-acid anion complex decreases the probability of detecting cerium(IV)-organic complexes. Whether or not the effect of increasing cerium(IV)-acid anion complex stability actually affects a change in mechanism with a change in acid is debatable. Muhammad and Rao (39,40) suggested that the mode of methanol oxidation is different in sulfuric and perchloric acids. However, as previously discussed, increasing the stability of the cerium(IV)-acid anion complex may decrease the stability of the cerium(IV)-substrate complex to a value which renders complex detection impossible by known methods.

CHELATE COMPLEX FORMATION

When considering carbohydrates or other polyols the possibility of chelate formation with cerium(IV) should be examined. There is general agreement (52-54) that the formation of chelate rings enhances the stability of coordination complexes. It has been established that five-membered rings are more stable than six-membered rings, provided no special resonance effects are involved, and that stability decreases rapidly when ring size becomes greater than six. It is also found that the equilibrium constants for complexes with polydentate ligands are larger than for complexes with monodentate ligands. The equilibrium constant is a measure of the standard free energy of a reaction,

$$\Delta F^{\circ} = -RT\ln K.$$

There is also an additional relationship between the standard free energy change and the enthalpy and entropy changes

$$\Delta F^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$$

so that an increase in an equilibrium constant results if ΔH° becomes smaller or if ΔS° becomes larger. It has been found that enthalpy changes in complex formation cannot, in general, account for the increase in equilibrium constants due to the chelate effect. Therefore, the chelate effect must be an entropy effect which can be calculated from measured values of the equilibrium constant and the enthalpies. It is found that chelation leads to higher entropy values, as predicted (52-54).

A qualitative, pictorial way of depicting the chelate effect is to consider the necessary interactions between the ligand and acceptor molecules or atoms. During nonchelate complex formation the ligand must displace one solvent molecule, usually water, from the metal ion so that the number of species in solution remains

constant. In chelate formation two or more solvent molecules are displaced by one ligand and the resulting number of more or less independent species increases, hence a positive increase in entropy for the system.

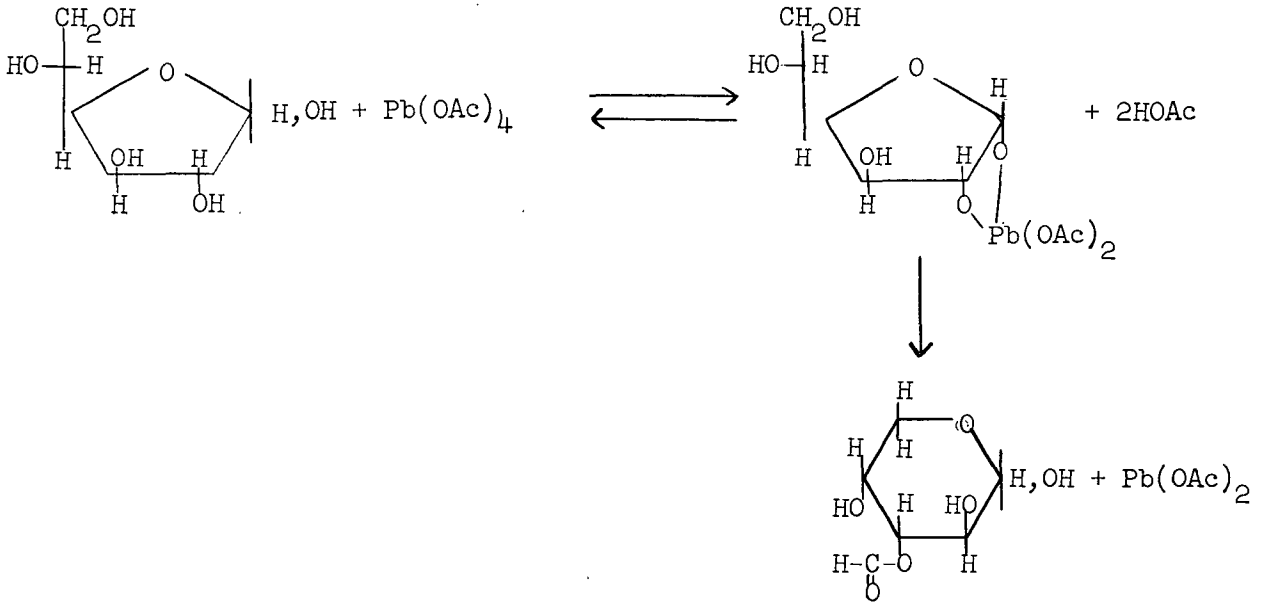
It is most important when considering evidence for chelation that thermodynamic values pertaining only to complex formation be used. In a reaction system such as is found in cerium(IV) oxidations based on the proposed mechanism, Equation (1), the activation energy, enthalpy and entropy refers to a sum which includes both the unimolecular and the equilibrium steps. The values would then pertain to an activated complex somewhere along the reaction coordinate between the cerium(IV)-substrate complex and the resulting substrate radical. Therefore, entropy values obtained from oxidation kinetics do not necessarily correlate with the chelate effect.

Because of the extra stability of chelate complexes it seems reasonable that such complexes will form whenever possible. Thus, it is probable that in oxidations of 1,2-oxygenated compounds the intermediate complex will be the preferred five-membered chelate ring. Of course, steric effects will, to a large extent, determine the possibility of chelate formation.

Criegee (55,56) first investigated the importance of chelate complexes in oxidations of 1,2-cyclohexanediols and 1,2-cyclopentanediols by lead tetraacetate. The cis-isomers were found to react faster than the corresponding trans-isomers and the cyclopentanediols were oxidized faster than cyclohexanediols. These results led to the postulated chelate complex which was favored by the geometry of the cis-isomer and greatly enhanced by the flattened, nearly coplanar orientation of cis-1,2-cyclopentanediol. The importance of chelate intermediates in lead tetraacetate oxidations of α-glycols is difficult to assess, since some compounds which require complex strain are not oxidized (57) and others

in which chelation is sterically impossible are oxidized (56). Besides this anomalous reactivity of lead tetraacetate with diols, it has been shown that such reactions are acid- and base-catalyzed (58,59), which generally is attributed to an acyclic reaction mechanism. The acyclic mechanism does not explain differences in reactivity of cis- and trans-isomers, so it must be assumed that lead tetraacetate is capable of oxidizing α-glycols by different mechanisms.

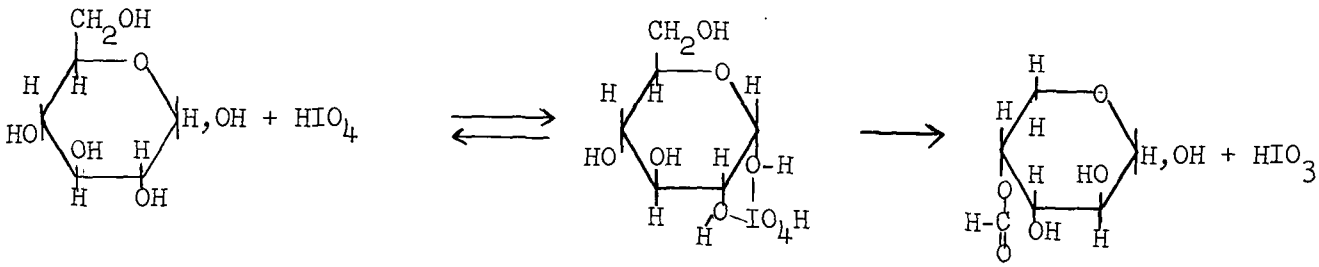
Lead tetraacetate oxidation of glucose is believed to involve a complex with the α-hydroxy hemiacetal glycol group. The nature of the complex is unknown, but it has been established that lead tetraacetate preferentially oxidizes the furanose form of glucose (60,61) and that the initial product is 3-O-formyl-D-arabinose. These results are consistent with the following mechanism:



in which the cyclic complex shown has not been proved.

Periodate oxidations of 1,2-diols are generally believed to involve cyclic intermediates (62,63). Unlike lead tetraacetate, periodate does not oxidize diols in which cyclic complex formation is impossible (63,64) or in which considerable strain would be necessary to form the cyclic complex (57). Glucose

oxidation by periodate is believed to involve a cyclic complex of periodate and the α-hydroxy hemiacetal group of the sugar. The pyranose form of glucose is known to be the reactive conformer as shown by nuclear magnetic resonance studies of the products obtained from the oxidations of deuterated D-glucose (61). From these studies in which the product, 4-O-formyl-D-arabinose, was identified it is reasonably certain that the mechanism is as follows:



(where the reactive form of the oxidant is not defined).

The importance of complexes in cerium(IV) oxidations has been established, but much less is known about the exact nature of these complexes. Unlike lead tetraacetate or periodate, cerium(IV) is capable of oxidizing alcohols, ketones, aldehydes, and acids as well as vicinal diols. Therefore, it seems reasonable that for cerium(IV) oxidations both acyclic and cyclic complexes are possible.

Offner (24,25) determined the equilibrium constants for complex formation by a spectrometric technique in both perchloric and nitric acid solutions. The alcohols studied were n-, sec-, and tert-butyl alcohols, diethylene glycol, and 1,3- and 1,4-butanediols. In each case it was found that the complex stoichiometry was one molecule of cerium(IV) per molecule of substrate complexed. The values of the equilibrium constants, which were much smaller in nitric than in perchloric acids, due to competing cerium(IV)-nitrate complexing, show relatively constant values for monohydric alcohols and 1,4-butanediol; whereas the values obtained for ethylene glycol and 1,3-butanediol, which can form five- and six-membered

chelate rings, respectively, are considerably higher. This increase in complex stability suggests the presence of chelate structures in these complexes.

Hintz (5,26) determined the equilibrium constant for complex formation from kinetic and spectrometric data for cyclohexanol, cis- and trans-1,2-cyclohexanediols, and trans-2-methoxycyclohexanol in perchloric acid. The data show approximately the same value for the equilibrium constants for cyclohexanol and trans-2-methoxycyclohexanol as have been determined for other monohydric alcohols by other workers. The values obtained for the cyclic 1,2-diols, however, are significantly higher, and in the range reported for glycerol, indicating possible chelate stabilization of the intermediate complexes. These data are summarized in Table III.

TABLE III

COMPLEX FORMATION CONSTANTS IN 1.0M PERCHLORIC ACID

Substrate	Temp., °C.	Complex Formation Constant, M^{-1}	Reference
Cis-1,2-cyclohexanediol	15.0	29.0	(5)
Trans-1,2-cyclohexanediol	15.0	18.0	(5)
Trans-2-methoxycyclohexanol	15.0	2.1	(5)
Cyclohexanol	15.0	2.9	(5)
Methanol	13.0	2.5	(40)
Ethanol	20.0	4.3	(16)
Glycerol	20.0	25.0	(47)

Hintz concluded that cis- and trans-cyclohexanediol are oxidized via chelate complexes and that the substitution of a methyl group for a hydroxyl hydrogen prevented chelation as indicated by the small equilibrium constant found for trans-2-methoxycyclohexanol.

The overall rates of cerium(IV) oxidations of trans-1,2-cyclohexanediol and trans-2-methoxycyclohexanol were found to be approximately the same despite great differences in the respective equilibrium constants. The similarity in overall rate is due to compensating differences in the rates of complex disproportionation. Littler and Waters (15) reported similar results obtained from studies of 2-methoxyethanol, and ethylene glycol in sulfate-containing media. Based on the similarity of the overall rates for both compounds the conclusion was drawn that ethylene glycol as well as its monomethyl ether are oxidized by an acyclic mechanism. Since no equilibrium constants were determined by Littler and Waters and the reactions were run in sulfuric acid where complex detection is difficult, it is suggested that the data of Hintz be given more credence concerning the importance of chelate complexes in diol oxidations by cerium(IV).

The importance of chelate intermediates in oxidation reactions has received much attention and except in the case of periodate has not been definitely established. The nature of cerium(IV) complexes is conceded to be affected by both the potential organic ligand and competing anion species. The importance of chelated cerium(IV)-glycol complexes is supported by the data of Offner (24, 25) and Hintz (5,26). The effect of methyl substitution for a hydroxylic hydrogen appears either to prevent chelation or to greatly reduce the stability of the chelate complex (5). In this study of the reactivity of cerium(IV) with various hydroxyl groups of carbohydrates the equilibrium constants for complex formation were all determined in perchloric acid to eliminate competition by the acid anion for coordination sites. In this media all results are comparable to those of Table III so that valid comparisons of complex stability can be made.

RESULTS AND DISCUSSION

DESCRIPTION OF COMPOUNDS STUDIED

The purpose of this thesis was to determine the relative reactivity of cerium(IV) with the various hydroxyl groups occurring in cellulose. This objective was accomplished by studying several monomeric models and one polymeric model for these functional groups. The reactivity of the reducing end-group was evaluated by a detailed study of the kinetics and products of D-glucose oxidation. Further information concerning hemiacetal (C_1) reactivity was obtained by kinetic studies of D-galactose, cellobiose, 2,3,4,6-tetra-O-methyl-D-glucose, 2-O-methyl-D-glucose, 2-O-methyl-D-galactose, 2-deoxy-D-glucose, 1,5-anhydro-D-glucitol, methyl β-D-glucopyranoside, and methyl β-D-galactopyranoside.

The model chosen for the anhydro-D-glucopyranose repeating unit of cellulose was Schardinger β-dextrin, Fig. 1. Schardinger β-dextrin is an α-1-4 linked cyclic polyglucan with seven monomeric units. Because of the solubility of this compound in aqueous media it provided an ideal model for anhydro-D-glucose units. The kinetics of cerium(IV) oxidation of anhydro-D-glucose units were determined using Schardinger β-dextrin. Product analysis studies of cerium(IV) oxidation of anhydro-D-glucose units were made using Schardinger β-dextrin and cellulose.

Methyl β-D-glucopyranoside and 1,5-anhydro-D-glucitol were selected as models for the nonreducing end of the cellulose molecule. The cerium(IV) oxidations of these compounds were studied kinetically.

Some of the model compounds for cellulose and cellulose itself contain glycosidic bonds; the stability of these bonds was demonstrated in the reaction medium under the conditions used in this study.

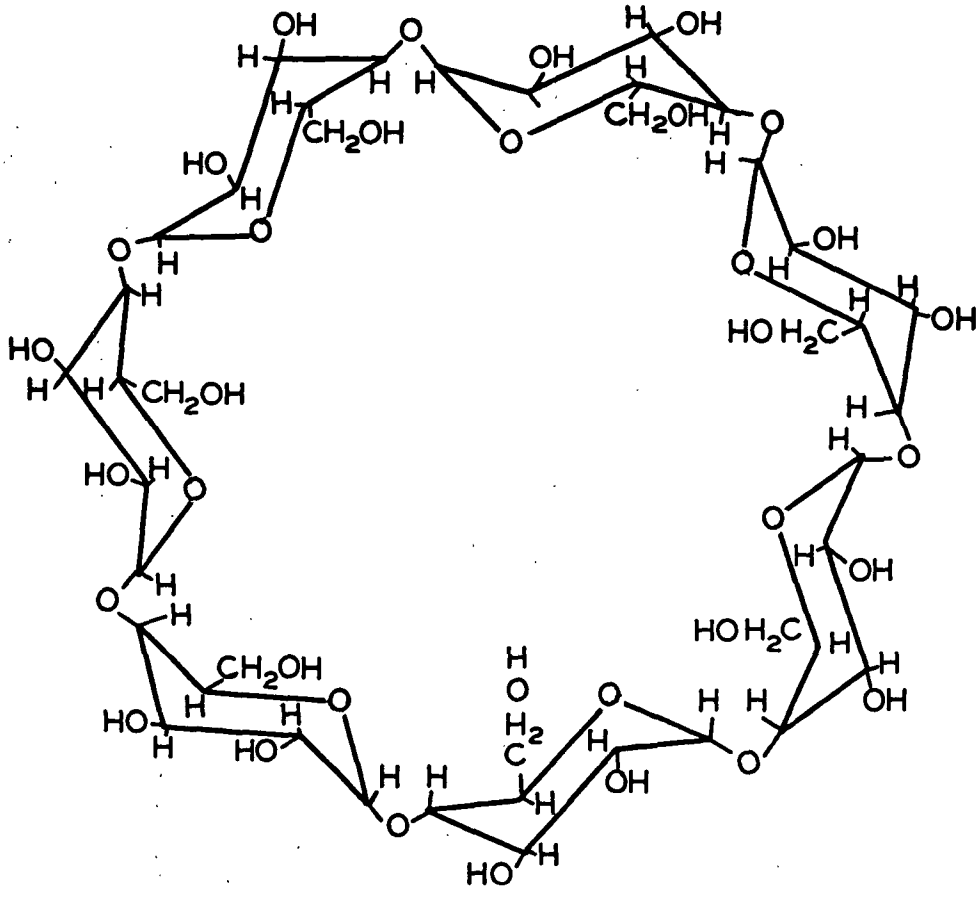


Figure 1. Schardinger β-Dextrin

DETERMINATION OF REACTION PRODUCTS AND STOICHIOMETRY

The products produced by the reaction of cerium(IV) with a two mole excess of glucose in perchloric or mixed sulfuric-perchloric acid are arabinose and formic acid. The identification of D-arabinose was made by comparative paper chromatography and by the properties of its diethyldithioacetal derivative.

The stoichiometry of glucose oxidation by cerium(IV) was proved by a quantitative study of reaction products. It was found that the yield of products was consistent with the following reaction:

$$2Ce(IV) + Glucose \longrightarrow 2Ce(III) + Arabinose + Formic\ Acid.$$

The method used to establish reaction stoichiometry involved the oxidation of two moles of glucose by one mole of cerium(IV) in perchloric acid. Under these conditions 25% of the original glucose, on a mole basis, will be converted to arabinose if the reaction is specific and proceeds by the above equation. Calculations using the assumed stoichiometry predict the percentage of glucose and arabinose in the product solution, based on total weight of carbohydrate, expressed as the sum of glucose and arabinose in the solution. The analytical results, obtained by quantitative paper chromatography (65), are compared to the predicted values in Table IV.

TABLE IV

QUANTITATIVE ANALYSIS OF CERIUM(IV)-GLUCOSE REACTION MIXTURE AND THEORETICALLY PREDICTED VALUES BASED ON THE EQUATION

$$2Ce(IV) + Glucose \longrightarrow 2Ce(III) + Arabinose$$

	Predicted	Found		
		1	2	Av.
Glucose, %[a]	78.28	76.76	76.18	76.41
Arabinose, %	21.72	23.24	23.82	23.59

[a]Percent based on total carbohydrate in system (glucose + arabinose).

The agreement between the predicted and observed values of arabinose and glucose concentrations confirmed the assumed stoichiometry.

The presence of formic acid as a product from cerium(IV) oxidation of glucose was confirmed by analyzing the distillate collected from a reaction mixture by the method of Feigl (66).

To ascertain whether the specific cleavage of the C_1-C_2 bond of glucose was characteristic of α-hydroxy hemiacetal groups the oxidation products of D-galactose and cellobiose were qualitatively determined by paper chromatography. For galactose, it was shown that, with a two mole excess of galactose with respect to cerium(IV), the only detectable product was lyxose corresponding to a specific C_1-C_2 cleavage. Under the same conditions, cellobiose yielded a disaccharide which on acid hydrolysis gave glucose and arabinose indicating the specific attack on the hemiacetal group. From these observations it was concluded that, under the conditions employed, cerium(IV) is a specific oxidant, similar to periodate or lead tetraacetate (61) in its action on ordinary reducing sugars.

The cerium(IV) oxidations of 2-O-methyl-D-glucose and 2-O-methyl-D-galactose were studied to determine the effect of 2-O-methyl substitution on the reactivity of the hemiacetal group. Qualitative paper chromatography of reaction mixtures from cerium(IV) oxidations of 2-O-methyl-D-glucose and 2-O-methyl-D-galactose demonstrated that the only detectable products were arabinose and lyxose, respectively. These results show that 2-O-methyl substitution does not change the site of aldose oxidation by cerium(IV).

The products of cerium(IV) oxidation of methyl β-D-glucopyranoside were qualitatively examined by paper chromatography. No arabinose was detected. The only detectable products were erythrose and either erythronic or glyoxylic acids, which are not resolved in the chromatographic systems used. The conclusion, based on the products observed from methyl β-D-glucopyranoside oxidation, is that glycosidation with O-methyl eliminates the attack of cerium(IV) at C_1, since no arabinose was found.

The reaction of cerium(IV) with anhydro-D-glucose was studied using two compounds. Since the kinetic model for anhydro-D-glucose was Schardinger β-dextrin, it was necessary to ascertain whether or not the reaction site in the model corresponded with the reaction site in authentic cellulose. This was done by qualitative analysis of hydrolyzates of cerium(IV)-oxidized Schardinger β-dextrin and cellulose, respectively. The results confirmed that erythrose and glyoxal were produced by hydrolysis of both oxidized polysaccharides. Once the identity of reaction products from cerium(IV)-oxidized Schardinger β-dextrin and cellulose was established, then quantitative product analysis studies were conducted using cellulose as the reductant.

The oxidation of cellulose for product analysis was carried out in an oxygen-free perchloric acid suspension. The anhydro-D-glucose unit concentration was twice the concentration of cerium(IV) on a mole basis. The oxidized cellulose was hydrolyzed in a solution of sulfurous and sulfuric acids and the erythrose was separated from glucose and fructose by preparative paper chromatography. The fructose was shown to be the result of acid epimerization of glucose under the hydrolysis conditions used [see reference (67) for a discussion of acid epimerization].

Figure 2 shows how the cleavage of the C_2-C_3 bond of an anhydro-D-glucose unit by cerium(IV) produces erythrose and glyoxal in the product hydrolyzate.

The presence of glyoxal was demonstrated by the isolation of its 2,4-dinitrophenylhydrazone from the hydrolyzates of oxidized Schardinger β-dextrin and cellulose. Identification was made by comparing thin-layer chromatographic mobilities with known glyoxal 2,4-dinitrophenylhydrazones in two solvent systems. The presence of glyoxal confirmed C_2-C_3 cleavage.

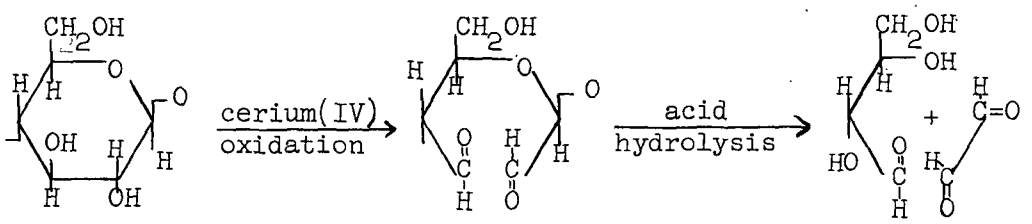


Figure 2. Products of Cerium(IV) Oxidation of Anhydro-D-Glucose

The quantitative determination of glucose, fructose, and erythrose was made using the cerium(IV) oxidation procedure of Smith and Duke (68). These workers established that there is an exact stoichiometric consumption of cerium(IV) for the oxidation of aldoses and ketoses to formic acid and CO_2 and developed equations predicting the cerium(IV) consumption for any aldose or ketose. Using these equations the amount of sugar present can be calculated from the measured cerium(IV) consumption.

A control experiment was conducted in which a synthetic mixture of glucose and erythrose was chromatographically separated and analyzed by the cerium(IV) procedure. The quantity of glucose in the control was accurately known, so the accuracy of the technique was indicated by comparing the known and found values for glucose. The authentic erythrose sample was a sirup of unknown concentration so that exact calibration with respect to this compound was impossible. The cerium(IV) consumption for a four-carbon aldose was assumed to be valid for erythrose. The results of the calibration experiment are given in Table V.

The oxidation of cellulose and Schardinger β-dextrin by cerium(IV) has been shown by product analysis to take place by cleavage of the C_2-C_3 bond. Assuming that this reaction consumes two moles of cerium(IV) per anhydro-D-glucose unit oxidized it is possible to predict the theoretical sugar composition of the hydrolyzate of an oxidized cellulose. The comparison of the theoretical

values with experimental values gives a minimum estimate of the extent to which the reaction follows the assumed course. Table VI shows the results obtained from the analysis of a cerium(IV)-oxidized-cellulose hydrolyzate. The analysis involved preparative paper chromatographic separation of hydrolyzate components and analysis by the cerium(IV) procedure of Smith and Duke (68).

TABLE V

RESULTS OF CONTROL EXPERIMENT USING CERIUM(IV) OXIDATION TO QUANTITATIVELY DETERMINE GLUCOSE AND ERYTHROSE[a]

	Moles Applied to Chromatogram	Moles Found in Chromatogram Eluate	Percent Recovered
Glucose	8.17×10^{-5}	8.02×10^{-5}	98.5
Erythrose[a,b]	2.87×10^{-5}	2.63×10^{-5}	91.5[c]

[a] Spotted simultaneously and isolated from same chromatogram as glucose.

[b] Concentration of original erythrose sample unknown; concentration estimated to be 75% erythrose.

[c] Percent recovered for erythrose is based on uncertain value for amount of erythrose applied.

TABLE VI

QUANTITATIVE ANALYSIS OF HYDROLYZATE OF CERIUM(IV) OXIDIZED CELLULOSE

	Percent Total Carbohydrate				Percent of Theory
	Run 1	Run 2	Av.	Theoretical	
Hexose[a]	92.8	92.6	92.7	82.25	
Erythrose	7.2	7.4	7.3	17.75	41.1

[a] Hexose includes glucose and fructose. Formation of fructose occurs during hydrolysis. Fructose is about 3% of total hexose.

The data do not prove that the reaction is specific or that the assumed stoichiometric relation, two moles cerium(IV) consumed per mole erythrose produced, is correct. It does show that at least 41% of the cerium(IV) consumed may be accounted for by the assumed stoichiometry. Furthermore, qualitative product analysis studies confirm C_2-C_3 cleavage with no detectable by-products.

The identity of erythrose in the hydrolyzates of cerium(IV)-oxidized cellulose was qualitatively demonstrated by paper and gas chromatography. Confirmation of erythrose was made by the isolation of erythrose and its subsequent reduction to erythritol, as evaluated by gas chromatography of the respective trimethylsilyl derivatives.

KINETICS OF CERIUM(IV) OXIDATIONS

ORDER OF REACTIONS WITH RESPECT TO CERIUM(IV) CONCENTRATION

In the presence of a large excess of organic substrate the rate of disappearance of cerium(IV) should be first order:

$$-d\,[Ce(IV)]/dt = k'\,[Ce(IV)] \qquad (18)$$

which on integration gives

$$\ln\left[[Ce(IV)]/[Ce(IV)]_o\right] = -k't \qquad (19)$$

It is known that the absorbance, $\underline{A}$, is a linear function of cerium(IV) concentration:

$$\ln(A/A_o) = -k't \qquad (20)$$

Therefore, plots of $\ln(\underline{A}/\underline{A}_o)$ versus time should be linear with slope $-\underline{k}'$.

The reactions of D-glucose, cellobiose, D-ribose, D-galactose, 2-$\underline{O}$-methyl-D-glucose, 2-$\underline{O}$-methyl-D-galactose, 2,3,4,6-tetra-$\underline{O}$-methyl-D-glucose,

2-deoxy-D-glucose, Schardinger β-dextrin, 1,5-anhydro-D-glucitol, methyl β-D-galactopyranoside, methyl β-D-glucopyranoside, methyl-4,6-di-O-methyl-β-D-glucopyranoside, and methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside all gave excellent pseudo-first-order kinetics in 1.0M perchloric acid. Reactions of D-glucose, D-galactose, cellobiose, and 2-O-methyl-D-galactose also gave pseudo-first-order kinetics in 0.25M sulfuric and 0.75M perchloric acid. The plots of $\ln(A/A_o)$ versus time for reactions of D-glucose, Schardinger β-dextrin, 1,5-anhydro-D-glucitol, and methyl β-D-glucopyranoside are given in Fig. 3 to 6, respectively. These plots are typical of all reactions studied in the course of this work.

The finding of linear logarithm plots shows that the order of reaction with respect to cerium(IV) is one. As a further confirmation of first-order dependence on cerium(IV), oxidations of glucose were conducted which showed that the pseudo-first-order rate constant is independent of initial cerium(IV) concentration. The results are given in Table VII.

TABLE VII

EFFECT OF INITIAL CERIUM(IV) CONCENTRATION ON THE PSEUDO-FIRST-ORDER RATE CONSTANT FOR OXIDATIONS OF GLUCOSE AT 20°C. IN 1.0M PERCHLORIC ACID

	Rate Constant, k', $sec.^{-1}$	
	Cerium(IV) Concn., M	
Glucose Concn., M	0.00196	0.00392
0.040	0.146	0.144
0.030	0.126	0.127
0.020	0.102	0.103
0.015	0.083	0.083
0.010	0.064	0.065

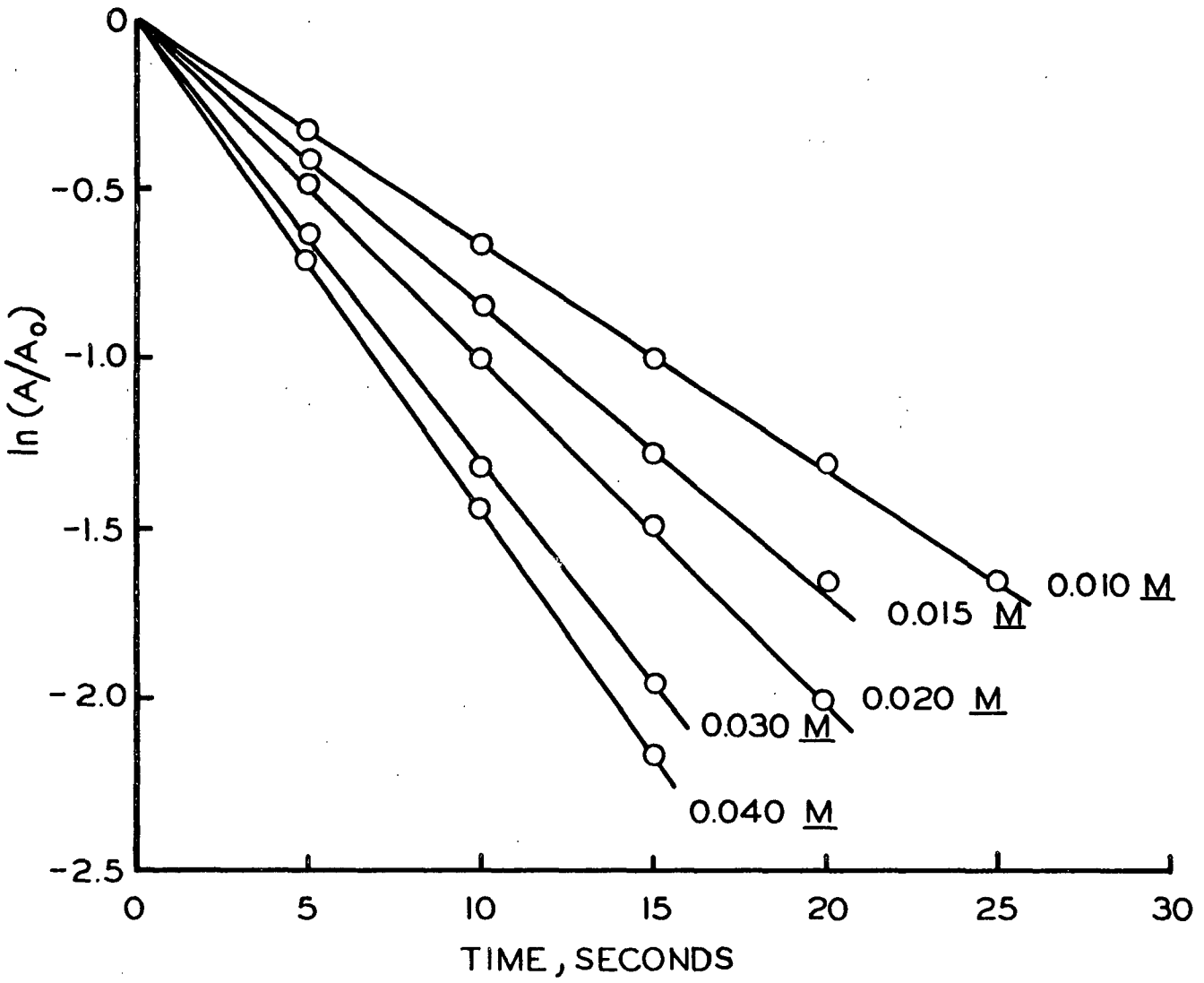


Figure 3. Pseudo-First-Order Reduction of Cerium(IV) by Glucose at 20°C. Initial Cerium(IV) Concn., 0.00196M. (Glucose Concentrations are Indicated)

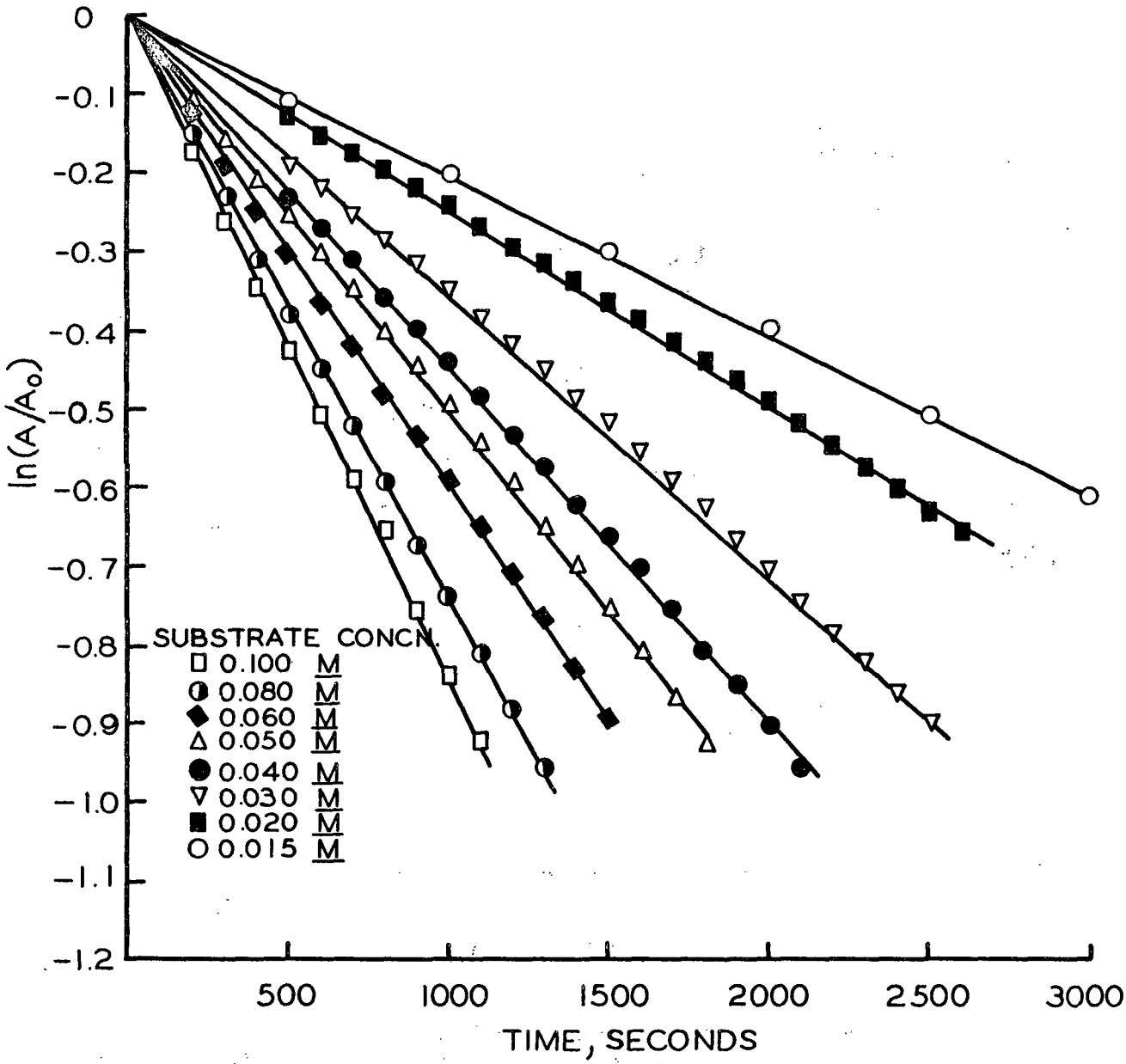


Figure 4. Pseudo-First-Order Reduction of Cerium(IV) by Schardinger β-Dextrin (Anhydro-D-Glucose Units) in 1.0M Perchloric Acid at 20°C. Initial Cerium(IV) Concn., 0.00196M

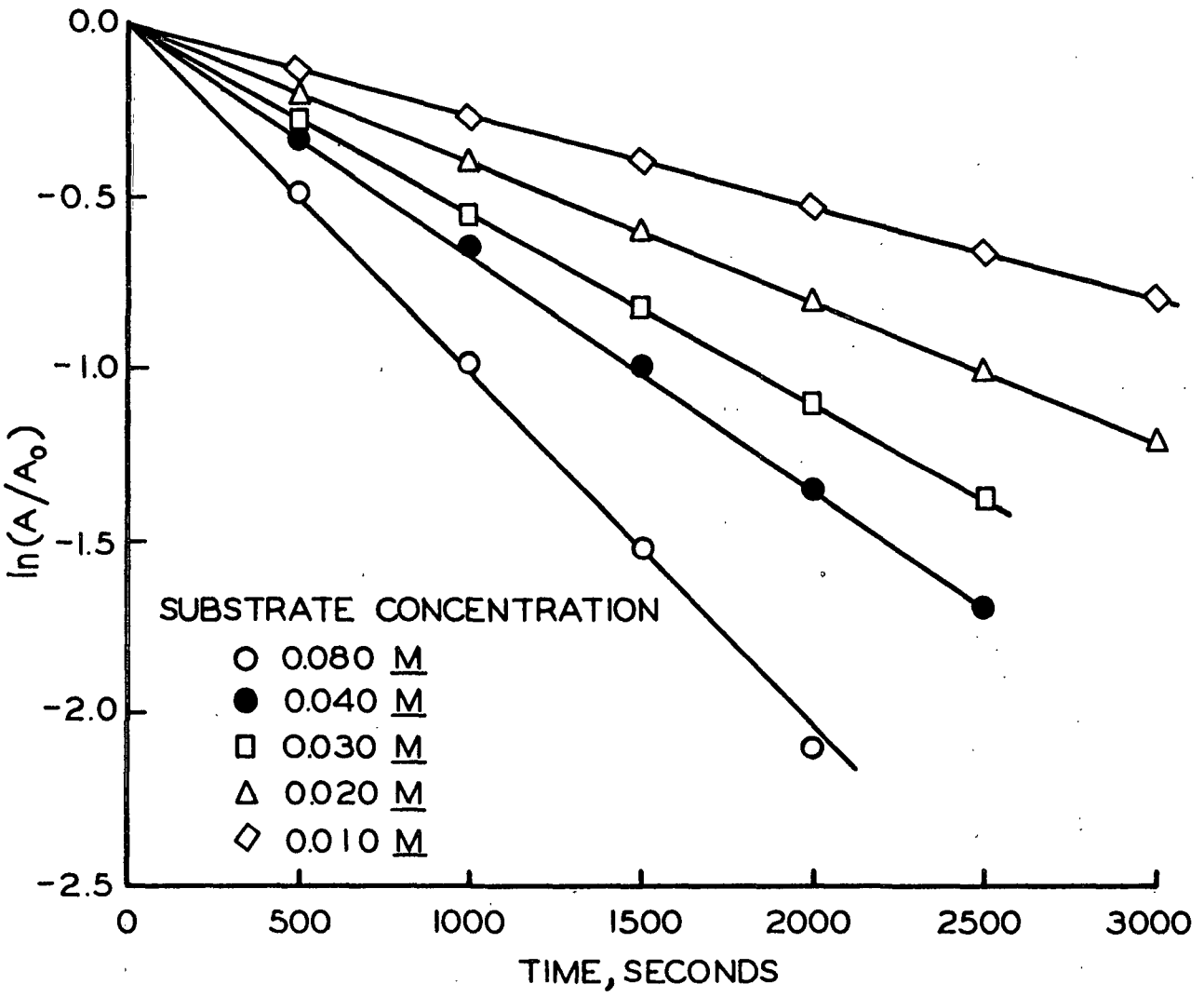


Figure 5. Pseudo-First-Order Reduction of Cerium(IV) by 1,5-Anhydro-D-Glucitol in 1.0M Perchloric Acid at 20°C. Initial Cerium(IV) Concn., 0.002M

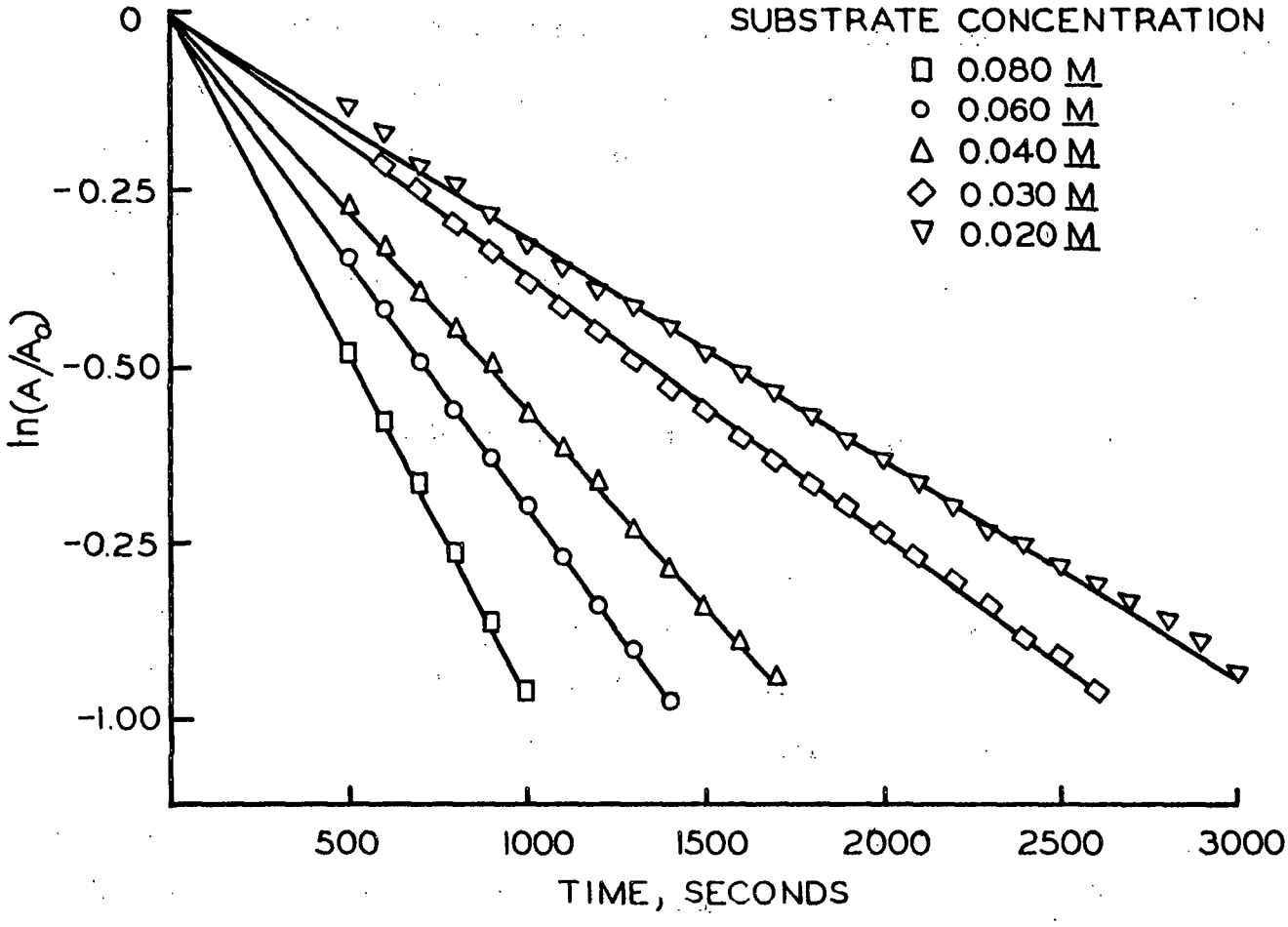


Figure 6. Pseudo-First-Order Reduction of Cerium(IV) by Methyl β-D-Glucopyranoside in 1.0M Perchloric Acid at 20°C. Initial Cerium(IV) Concn., 0.00196M

EFFECT OF OXYGEN ON KINETICS

Dissolved oxygen is known to affect the rates of organic oxidations by cerium(IV). Hintz (5) reported a drastic effect of dissolved oxygen in oxidations of cyclohexanediols in 1.0M perchloric acid. He found that plots of the logarithm of absorbance versus time were not linear when no precautions were taken to eliminate dissolved oxygen from the system. In the present work the oxygen problem was anticipated; so all reactions in perchloric acid were purged with dry nitrogen to reduce dissolved oxygen concentrations. Figure 7 shows the effect of dissolved oxygen on the slope of pseudo-first-order plots for methyl β-D-glucopyranoside. The effect of dissolved oxygen in this reaction system was to increase the rate of disappearance of cerium(IV); however, no deviation from linearity was observed.

ORDER OF REACTIONS WITH RESPECT TO SUBSTRATE CONCENTRATION: EVIDENCE FOR COMPLEX FORMATION

Kinetic Evidence for Complex Formation

As discussed in a previous section, determination of the dependence of the pseudo-first-order rate constant on substrate concentration provides a means for identifying the various reaction mechanisms.

For reactions proceeding through intermediate complexes, the pseudo-first-order rate constant is given by Equation (6) which predicts that a plot of k' versus R will be nonlinear, concave downward, and pass through zero. The reciprocal plot, $1/k'$ versus $1/R$, however, will be linear and the equilibrium constant for complex formation, K, and the disproportionation rate constant, k, can be calculated from the slope and intercept. For the direct oxidation mechanism and certain variations of the intermediate complex mechanism as

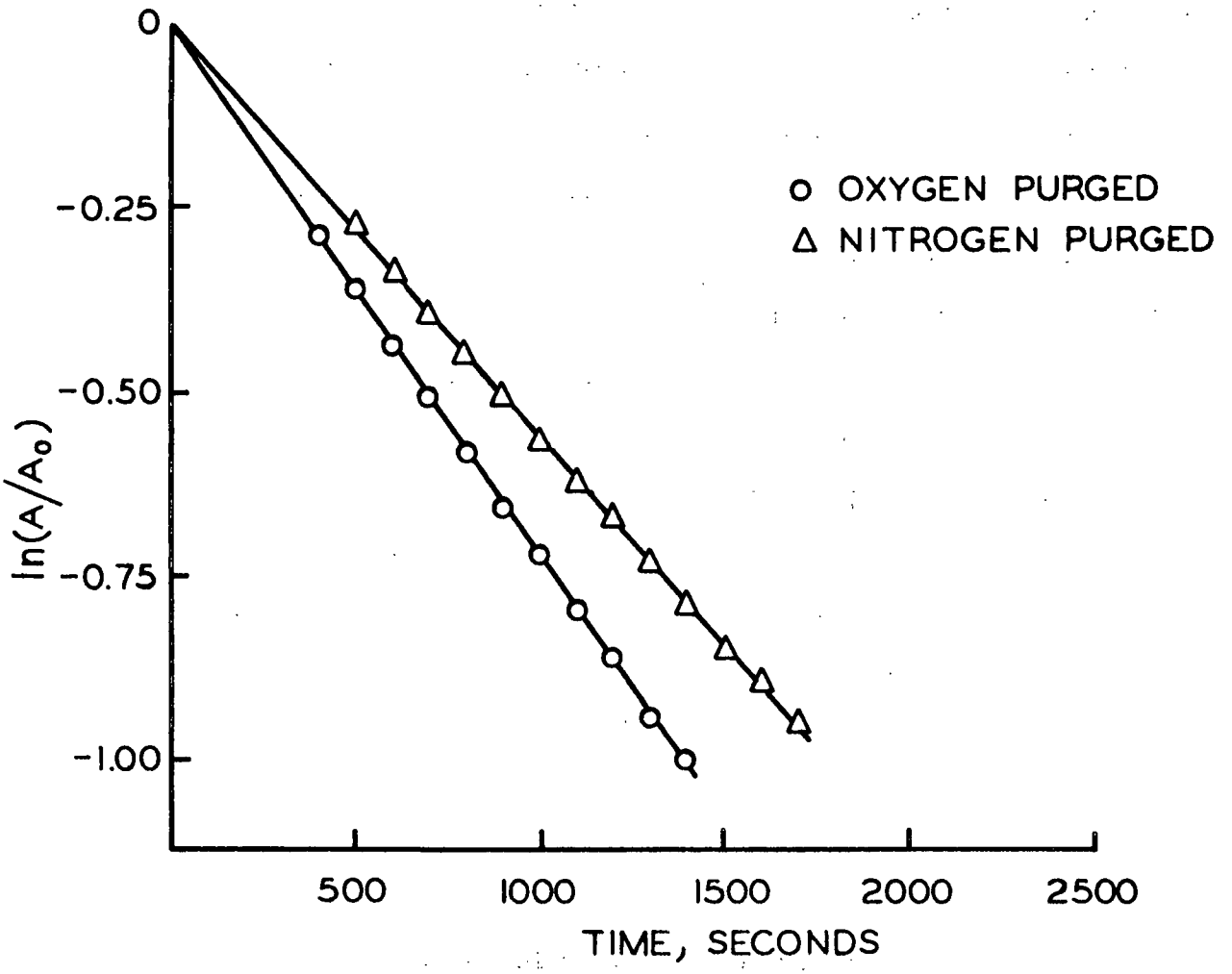


Figure 7. Effect of Oxygen on the Reaction of 0.040M Methyl β-D-Glucopyranoside in 1.0M Perchloric Acid at 20°C. Initial Cerium(IV) Concn., 0.00196M

previously described, a plot of k' versus R will be linear with slope k_{II} and zero intercept.

All compounds investigated in 1.0M perchloric acid, for which various substrate concentrations were studied, gave plots of k' versus R which were curved, concave downward, and had zero intercepts. This behavior is shown in Fig. 8 and 9 for D-glucose, Schardinger β-dextrin, 1,5-anhydro-D-glucitol, and methyl β-D-glucopyranoside oxidations, respectively. The definite curvature of the plots indicates that these compounds are oxidized by mechanisms involving intermediate complex formation. Further evidence for the participation of intermediate complexes was obtained from the linear reciprocal plots, Fig. 10 and 11. The equilibrium constants for complex formation and the complex disproportionation rate constants calculated from the slopes and intercepts of these plots are given in Table VIII.

Spectrometric Evidence for Complex Formation

As discussed in the Introduction, Ardon (16) devised a method which permits the determination of complex formation constants, K, from spectrometric data. The spectrometric method depends on the estimation of intermediate complex concentration by spectrometric measurement and is independent of the kinetic method. Figure 12 shows the reciprocal plots of spectrometric data from which the equilibrium constant for complex formation for Schardinger β-dextrin, 1,5-anhydro-D-glucitol, and methyl β-D-glucopyranoside were calculated. These values are presented in Table VIII for comparison with results obtained by analysis of kinetic data. Some data from the literature are also given in Table VIII.

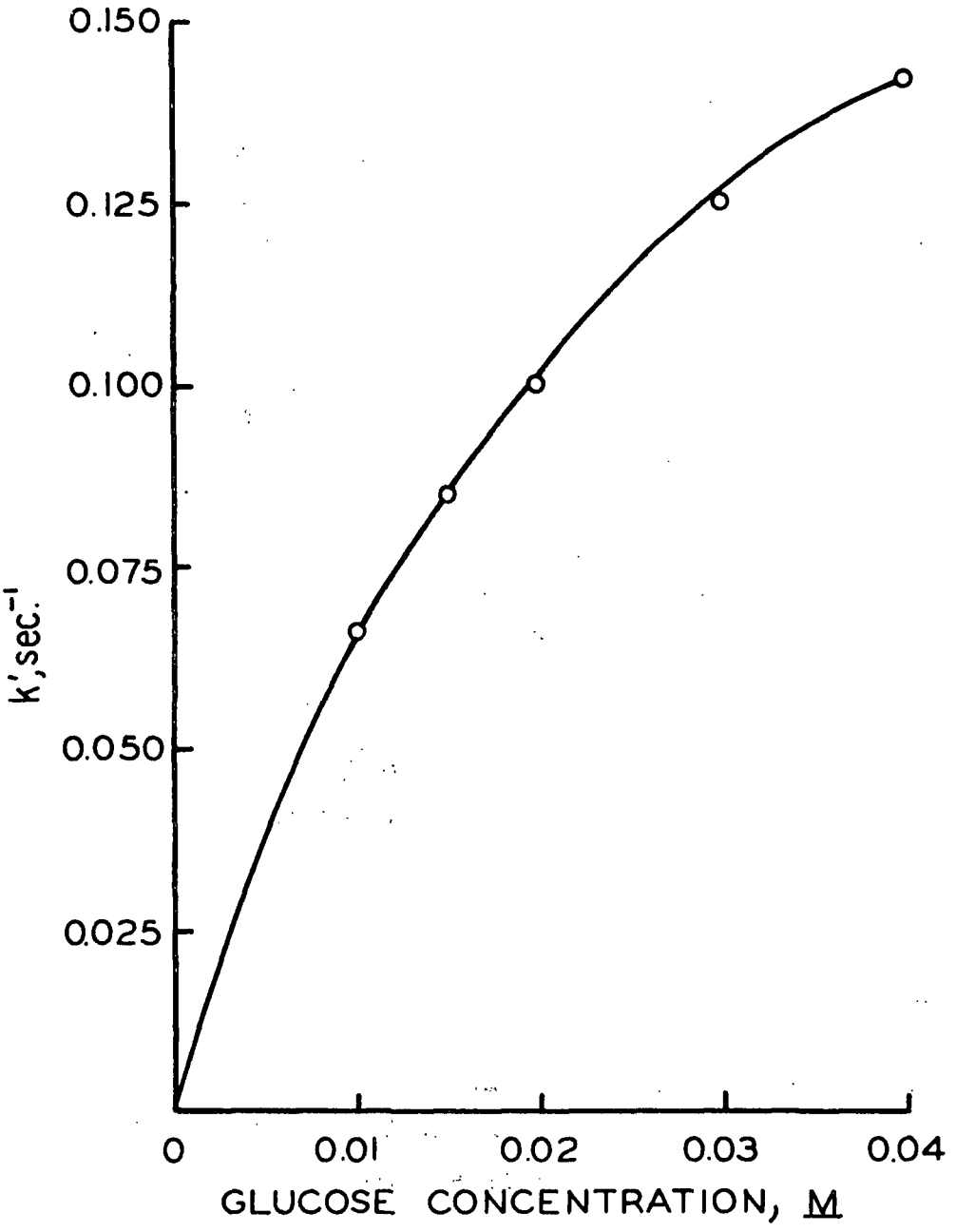


Figure 8. Effect of Glucose Concentration on the Pseudo-First-Order Rate Constant at 20 °C. Initial Cerium(IV) Concn. 0.002M

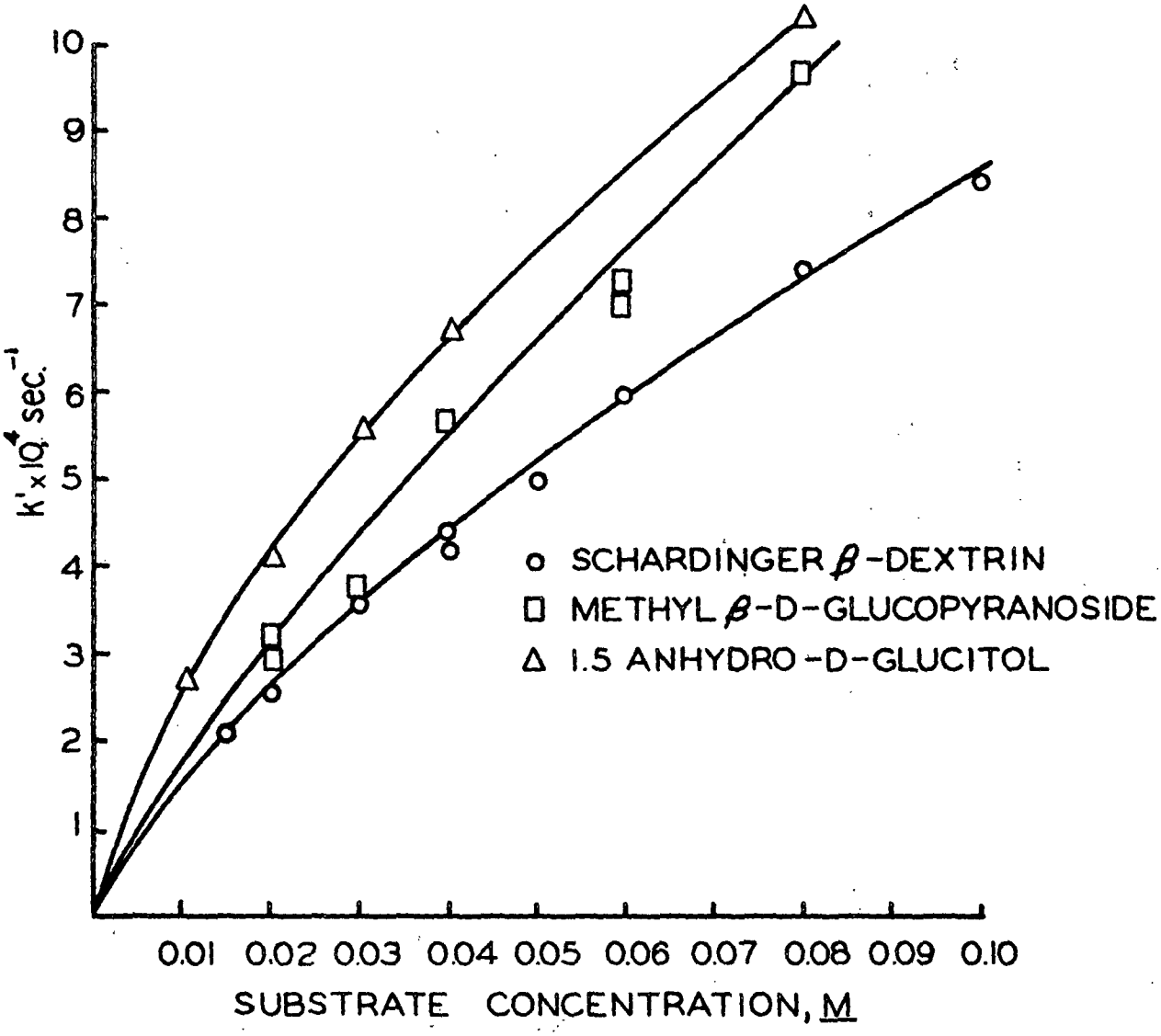


Figure 9. Effect of Substrate Concentration on Pseudo-First-Order Rate Constant at 20°C.

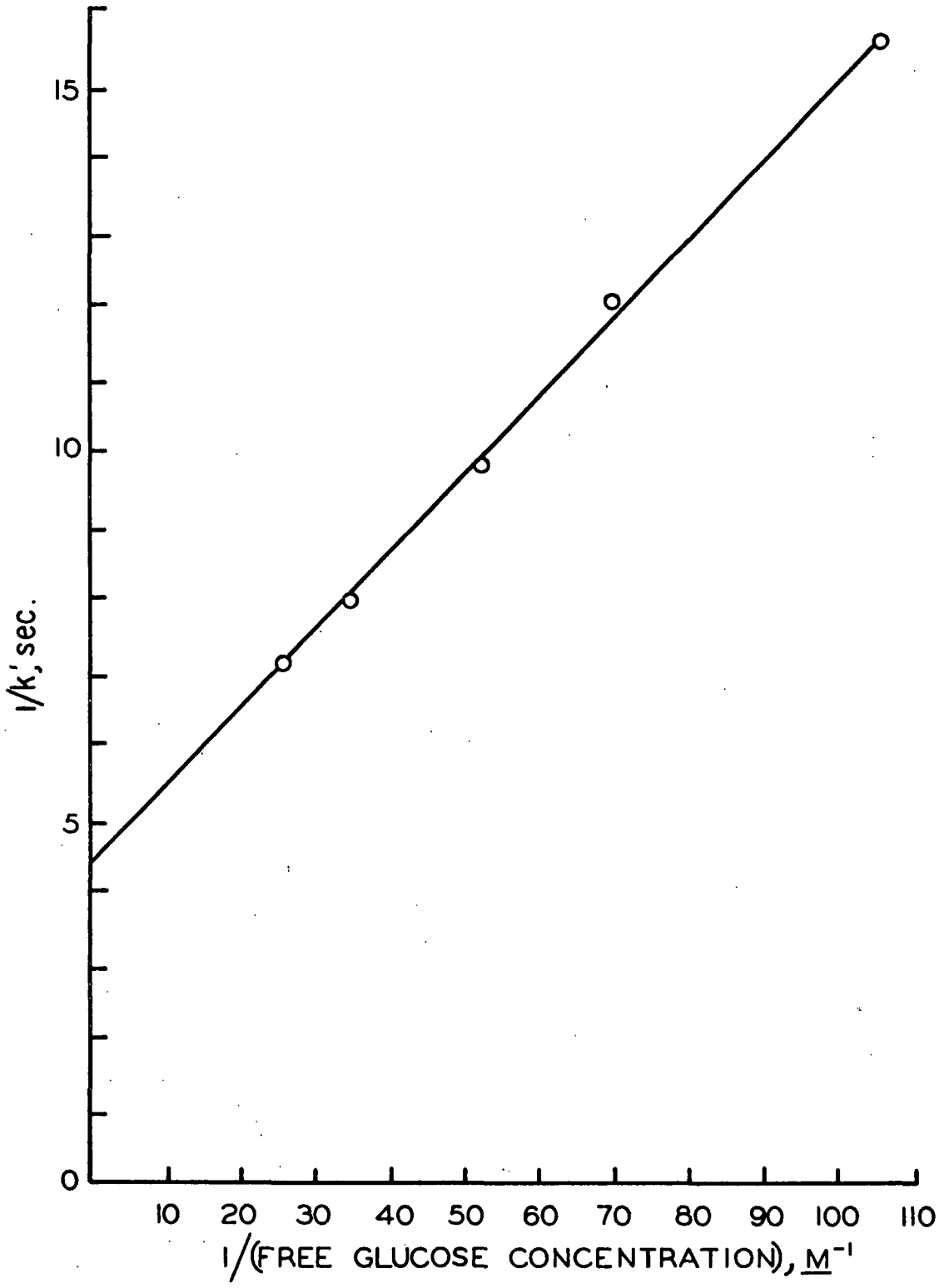


Figure 10. Reciprocal Plot for Reactions of Glucose with Cerium(IV) in 1.0M Perchloric Acid at 20°C.

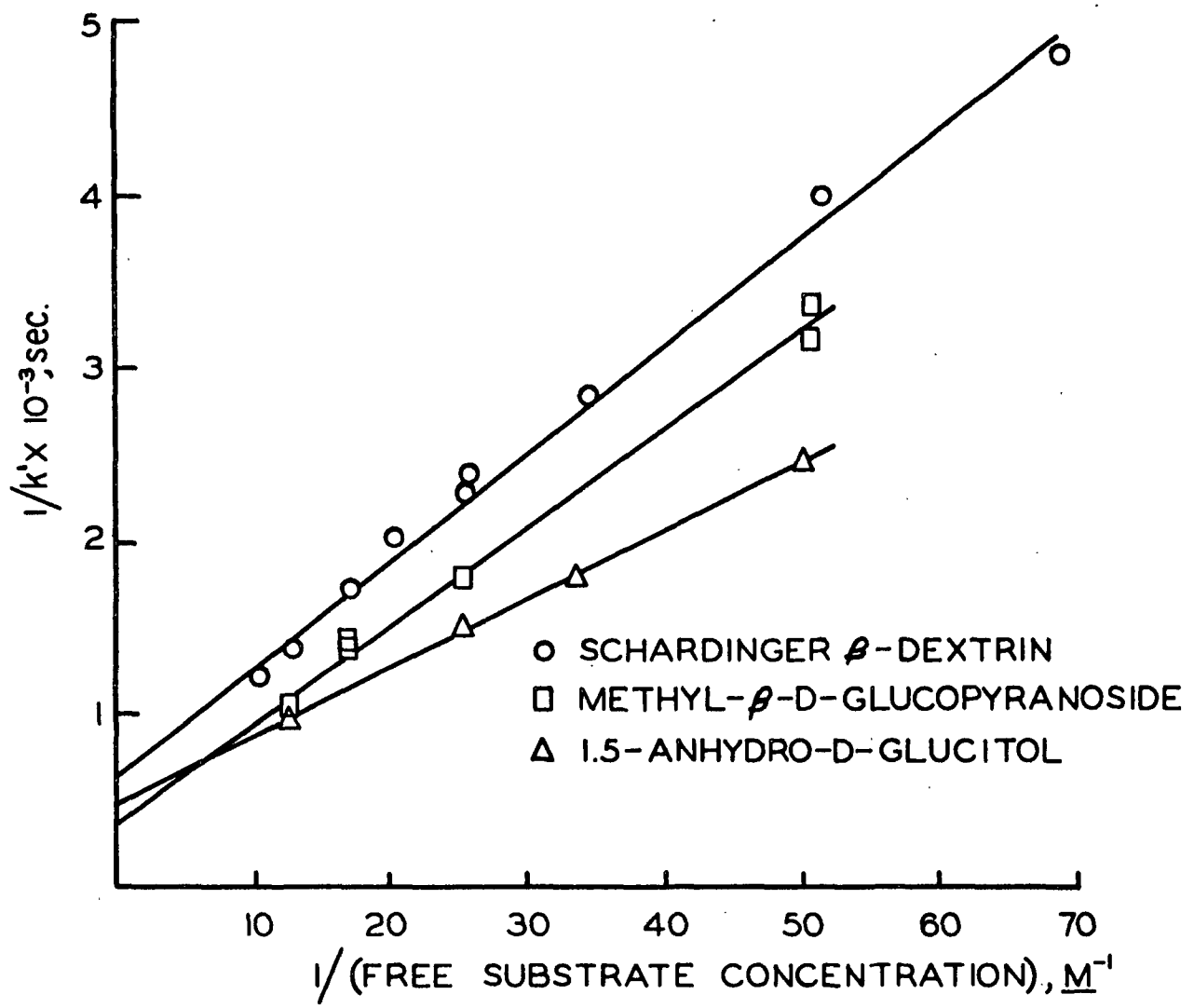


Figure 11. Reciprocal Plots for Reactions in 1.0M Perchloric Acid at 20°C.

TABLE VIII

EVIDENCE FOR COMPLEX FORMATION IN 1.0M PERCHLORIC ACID: COMPLEX FORMATION CONSTANTS AND RATE CONSTANTS FOR COMPLEX DISPROPORTIONATION

	Temp., °C.	Complex Formation Constant, K, M^{-1} Spectrometric Data	Complex Formation Constant, K, M^{-1} Kinetic Data	Disproportionation Rate Constant k, $min.^{-1}$	Reference
cis-1,2-Cyclohexanediol	15.0	29.3	29.0	0.85	(5)
trans-1,2-Cyclohexanediol	15.0	18.6	18.0	0.36	(5)
trans-2-Methoxycyclohexanol	15.0	2.9	2.1	3.3	(5)
Cyclohexanol	15.0	3.9	2.9	0.13	(5)
Methanol	13.0	--	2.5	0.23	(40)
Methanol	20.0	--	1.5	0.62	(40)
Ethanol	20.0	4.3	4.3	0.4	(16)
Glycerol	20.0	--	25.0	0.83	(47)
Glucose	20.0	--	39.4	14.04	This work
1,5-Anhydro-D-glucitol	20.0	12.7	12.7	0.12	This work
Anhydro-D-glucose[a]	20.0	9.0	10.3	0.09	This work
Methyl β-D-glucopyranoside	20.0	9.4	6.2	0.16	This work

[a] Schardinger β-dextrin.

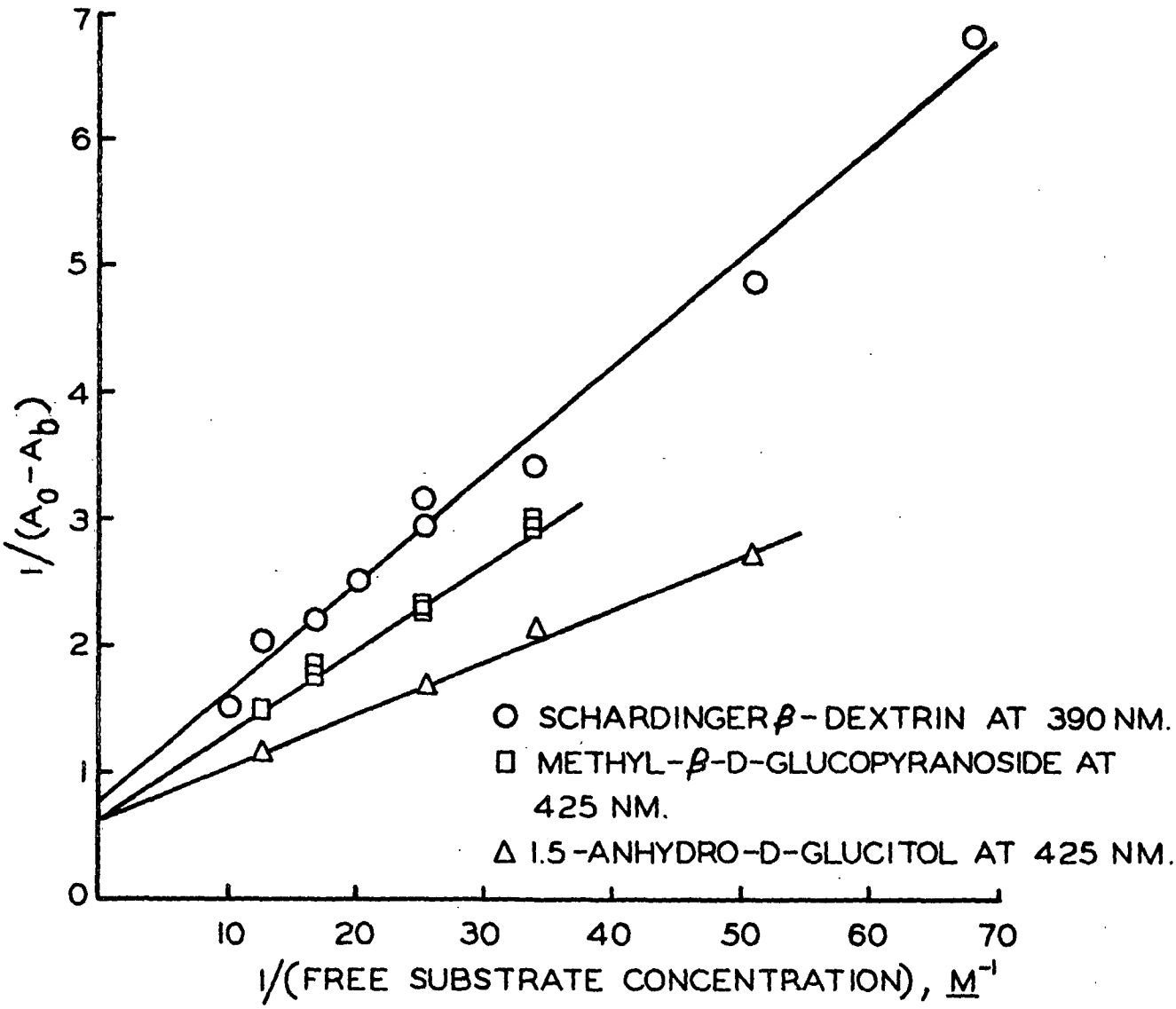


Figure 12. Reciprocal Plots of Spectrophotometric Data for Reactions in 1.0M Perchloric Acid at 20°C.

KINETICS OF REACTIONS OF GLUCOSE DERIVATIVES: EVIDENCE FOR COMPLEX PARTICIPATION

The relatively high reactivity of glucose as compared with methyl β-D-glucopyranoside, prompted the study of several C_1-C_2 substituted glucose derivatives in an attempt to evaluate the nature of the cerium(IV)-reducing sugar interaction. The effect of varying the C_1 and C_2 substituents of glucose was compared by kinetic studies of glucose, 2-O-methyl-D-glucose, 2-deoxy-D-glucose, 1,5-anhydro-D-glucitol, methyl β-D-glucopyranoside, and Schardinger β-dextrin (anhydro-D-glucose) under identical conditions. The results of these studies are tabulated in Table IX.

The results show that all of the nonreducing* compounds studied: 1,5-anhydro-D-glucitol, methyl β-D-glucopyranoside, and anhydro-D-glucose, are oxidized at rates significantly lower than the rates for the reducing compounds: glucose, 2-O-methyl-D-glucose, and 2-deoxy-D-glucose. It has also been shown that cerium(IV) oxidations of the reducing compounds, glucose and 2-O-methyl-D-glucose, yield arabinose indicating that the reactive site involves C_1; whereas with oxidations of nonreducing compounds no products indicating attack at C_1 have been detected. This leads to the conclusion that the hydroxyl on C_1 is the most reactive site of glucose or other reducing sugars.

The importance of complex formation in cerium(IV) oxidation of glucose has been established by kinetic studies described in an earlier section. The magnitude of the apparent equilibrium constant for glucose oxidation, $39.4\underline{M}^{-1}$, is taken as evidence for the participation of a chelated intermediate probably involving the oxygen atoms of C_1 and C_2. Studies of the compounds listed in Table IX show that the reactivity of glucose derivatives is, as would be

*The terms reducing and nonreducing refer to the presence or absence of the hemiacetal group at C_1 of the glucose derivative.

predicted, dependent on the presence of the unsubstituted C_1 hydroxyl and greatly enhanced by the presence of oxygen at the C_2 position. The fact that both glucose and 2-O-methyl-glucose yield the same reaction product, arabinose, suggests that both compounds are oxidized by similar mechanisms. No evidence was obtained for the participation of chelate complexes in cerium(IV) oxidation of 2-O-methyl-glucose, but the similarity of rate and identity of products to those of glucose oxidation definitely establish the importance of oxygenation on C_2. Various mechanistic considerations concerning the effect of O-methyl substitution on diol oxidations by cerium(IV) are discussed in a later section.

TABLE IX

REACTION RATES OF SELECTED CARBOHYDRATE DERIVATIVES WITH CERIUM(IV)[a] IN 1.0M PERCHLORIC ACID[b]

Compound[c]	Pseudo-First-Order Rate Const., $sec.^{-1}$	Relative Rate[d]
Glucose	0.0855	360
2-Deoxy-D-glucose	0.00294	12.4
2-O-Methyl-D-glucose	0.431	1860
2,3,4,6-Tetra-O-methyl-D-glucose	0.454[e]	--
Galactose	0.175	736
2-O-Methyl-D-galactose	0.297	1250
Cellobiose	0.05006	212
Ribose	0.1747	740
1,5-Anhydro-D-glucitol	0.000360	1.5
Schardinger β-dextrin[f]	0.000236	1
Methyl β-D-glucopyranoside	0.000237	1
Methyl β-D-galactopyranoside	0.0011	--

[a] Initial cerium(IV) concentration, 0.00196M.
[b] Reductant concentration, 0.040M.
[c] Temperature 15°C.
[d] Based on anhydro-D-glucose.
[e] Temperature for reaction of 2,3,4,6-tetra-O-methyl-D-glucose, 20°C.
[f] Anhydro-D-glucose.

DISCUSSION OF COMPLEX FORMATION DATA

As discussed in the Introduction, cerium(IV) exists as a number of hydrated ionic species in aqueous perchloric acid. Some of these ions are believed to be Ce^{4+}, $CeOH^{3+}$, $CeOH_2^{2+}$, and $(Ce\text{-}O\text{-}Ce)^{6+}$. The concentration of dimeric forms increases with increasing cerium(IV) concentration and with increasing pH. However, at the high acidity and low cerium(IV) concentrations usually used for kinetic studies [below 0.01M cerium(IV)] the concentration of dimers is very low (32). Hydrolysis equilibria between monomeric cerium(IV) species are important at the acidities used for kinetic studies. As a consequence, it has been shown (16,40,47) that rates of cerium(IV) oxidations in perchloric acid increase with increasing acid concentration. It was concluded (40) that the increased rates of oxidation were due to the increased concentration of hydrated Ce^{4+} resulting from displacement of the equilibrium, Equation (21), to the left by increased acid concentration.

$$Ce^{4+} + H_2O \underset{}{\overset{K_h}{\rightleftharpoons}} CeOH^{3+} + H^+ \qquad (21)$$

Since the equilibrium constants for complex formation obtained by kinetic or spectrometric methods are based on total cerium(IV) concentration, they are actually apparent equilibrium constants which depend on acid concentration due to the above hydrolysis equilibrium. Muhammad and Rao (40) assumed the above equilibrium and derived an equation, Equation (22), which relates the apparent equilibrium constant, K, to the true equilibrium constant for complex formation, $\bar{K}$, and were able to verify the theory for ceric perchlorate oxidations of methanol. Examination of the equation reveals that, under any given experimental

$$\bar{K} = K(1 + K_h/[H^+]) \qquad (22)$$

conditions, the apparent equilibrium constant differs from the true value by a constant. Therefore, it is valid to compare apparent equilibrium constants

obtained for various reductants when experimental conditions are identical with respect to acid and cerium(IV) concentrations.

In Table VIII, values for apparent equilibrium constants for reactions in 1.0M perchloric acid are summarized. A substantial increase in complex stability is apparent for compounds containing diol groups as compared to compounds containing only one hydroxyl. This increased stability for diols, as evidenced by large equilibrium constants, indicates the formation of chelate complexes with α-glycols. Thus, Hintz (5) concluded that cis- and trans-1,2-cyclohexanediols are oxidized by chelated intermediate complexes, due to the large equilibrium constants found for these compounds, whereas the similarity of equilibrium constants found for trans-2-methoxycyclohexanol with those found for monohydric alcohols suggested that the methyl group prevents chelation. The possibility of chelate formation involving the methoxyl oxygen cannot be excluded on the basis of equilibrium constant data. Hintz (5) pointed out that the methoxyl group might simply reduce chelate stability rather than preventing chelation entirely.

Considering the disproportionation rate constants given in Table VIII it can be shown that the overall rate constants, kK, for trans-1,2-cyclohexanediol, and trans-2-methoxycyclohexanol are nearly identical. This behavior has been interpreted as evidence that chelate formation is not a necessary requirement for cerium(IV) oxidations of diols (5,26) and it has been predicted (5) that cerium(IV) could oxidize compounds such as trans-9,10-dihydrophenanthrene-9,10-diol and trans-9,10-decalindiol, in which chelate complex formation is difficult or impossible, at rates comparable to the corresponding cis-isomers.

Further information concerning the effect of methoxyl on cerium(IV)-alcohol complexing was obtained in this study. In Table X are summarized the results of kinetic experiments involving methyl 2,3,4,6-tetra-O-methyl-β-D-

glucopyranoside, methyl 4,6-di-O-methyl-β-D-glucopyranoside, methyl β-D-glucopyranoside, Schardinger β-dextrin (anhydro-D-glucose), 2-O-methyl-D-glucose, 2-deoxy-D-glucose, and glucose. Anhydro-D-glucose, which is nonreducing and contains no methoxyl, is oxidized at the same rate as methyl β-D-glucopyranoside and at about the same rate as methyl 4,6-di-O-methyl-β-D-glucopyranoside. Since the magnitude of equilibrium constants for complex formation determined for anhydro-D-glucose and methyl β-D-glucopyranoside (Table VIII) indicate the participation of chelate intermediates, it is probable that the diol-containing compound, methyl 4,6-di-O-methyl-β-D-glucopyranoside, is also attacked by chelate complex formation with the unsubstituted C_2-C_3 hydroxyls. Substituting methyl for hydroxyl hydrogen decreases the rate of oxidation by cerium(IV). Thus, methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside is oxidized at one-fifteenth the rate of methyl 4,6-di-O-methyl-β-D-glucopyranoside (Table X). This shows that methoxyl groups are less reactive than hydroxyl groups toward cerium(IV).

TABLE X

EFFECT OF O-METHYL SUBSTITUTION ON PSEUDO-FIRST-ORDER RATE CONSTANTS FOR CERIUM(IV) OXIDATIONS AT 15°C.

Compound[a]	Pseudo-First-Order Rate Constant, $sec.^{-1}$	Relative Rate
Methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside	0.0000113	0.048
Methyl 4,6-di-O-methyl-β-D-glucopyranoside	0.000164	0.7
Methyl β-D-glucopyranoside	0.000237	1
Schardinger β-dextrin[b]	0.000236	1
2-O-Methyl-D-glucose	0.431	1860
2-Deoxy-D-glucose	0.00294	12.4
Glucose	0.085	360

[a]Substrate concentration 0.040M in all cases.

[b]Anhydro-D-glucose.

As evidence previously discussed points out, the C_1 or hemiacetal hydroxyl of glucose is much more reactive than any of the other hydroxyl groups. Studies of the reactions of glucose and 2-O-methyl-D-glucose show that both yield arabinose, indicating reaction with the highly reactive C_1 hydroxyl and cleavage of the C_1-C_2 bond. However, the rate of 2-O-methyl-D-glucose oxidation is greater than the rate of glucose oxidation. Similar results were obtained by Hintz (5) and Littler and Waters (15). Hintz found that trans-1,2-cyclohexanediol and trans-2-methoxycyclohexanol were oxidized at about the same rate and Littler and Waters found similar rates for cerium(IV) oxidations of ethylene glycol and 2-methoxyethanol. Considering the systems studied by Hintz (5) and Littler and Waters (15) it can be seen that in both cases the reactive site present contained either an unsubstituted diol or an α-methoxyalcohol group. In simple systems containing only a diol or a monomethylated diol the reaction is restricted to the oxygenated site. For such a restricted system Hintz (5) postulated that the diol is oxidized via stable chelate intermediates and that α-methoxyalcohols are oxidized at about the same overall rate, but by means of a less stable acyclic intermediate complex. The glucose and 2-O-methyl-D-glucose systems are analogous to the trans-1,2-cyclohexanediol and trans-2-methoxycyclohexanol systems in that the highly reactive hemiacetal site restricts the point of attack of cerium(IV) to the C_1 hydroxy regardless of the substituent on C_2 as indicated by the reactivities of glucose, 2-O-methyl-D-glucose, 2,3,4,6-tetra-O-methyl-D-glucose, and 2-deoxy-D-glucose (Table IX). Again, in the restricted glucose and 2-O-methyl-D-glucose systems, little difference in relative rates were observed indicating that both the cyclic (glucose) and acyclic (2-O-methyl-D-glucose) cerium(IV) complexes can cleave the C_1-C_2 bond at similar rates.

The reactions of methyl β-D-glucopyranoside, and methyl-4,6-di-O-methyl-β-D-glucopyranoside, compounds which contain unrestricted sites of both diol and

α-methoxyalcohol types, were found to be oxidized at rates essentially identical to anhydro-D-glucose, which contains only hydroxyl sites and has been found to be oxidized by C_2-C_3 cleavage corresponding to chelate formation with the diol group. Furthermore, methyl β-D-glucopyranoside produced no detectable arabinose, the product of C_1-C_2 cleavage, indicating attack only at available diol groups.

These results are interpreted to provide substantiation to the postulate of Hintz (5) that the stability of the intermediate complex determines the reaction site and mechanism. When equally accessible unrestricted sites of the diol and α-methoxyalcohol types are present in the same molecule, the reaction mechanism involving chelation of cerium(IV) with diol groups predominates because of the increased stability of the chelate, which can be measured by determination of complex formation constants. With restricted reaction sites such as α-methoxy-alcohols and α-methoxyhemiacetals the reaction involves a less stable intermediate, probably acyclic, which is capable of more rapid disproportionation so that the overall rates of cerium(IV) consumption by both mechanisms are approximately equal.

Comparing the rates of cerium(IV) oxidation of the various compounds in Tables IX and X shows that 2-O-methyl-, and 2-hydroxy-aldoses are highly reactive; whereas, 2-deoxy-D-glucose, which has no oxygen on C_2, is oxidized at a rate lower than the C_2 oxygenated hemiacetals, but greater than the nonreducing models (e.g., anhydro-D-glucose, methyl β-D-glucopyranoside, 1,5-anhydro-D-glucitol). Since it is known that cerium(IV) oxidations of monohydric alcohols yield the corresponding carbonyl compounds and do not cleave carbon-carbon bonds and that 1,2-oxygenated systems are oxidized by carbon-carbon bond cleavage, it seems reasonable that the presence of oxygen on both carbon positions is necessary for disproportionation of the primary bond. Evidence indicates that in the case of diols both oxygen

atoms participate in a chelate complex with cerium(IV). On the other hand, for α-methoxyalcohols acyclic intermediates are indicated. The presence of the methoxyl oxygen in the acyclic complex may serve to stabilize a developing radical in the disproportionation step, permitting the formation of a transition state which is geometrically similar to the transition state encountered in disproportionation of the chelate complex in diol oxidations. This concept is discussed in the following section.

Hintz (5) found that while the equilibrium constant for complex formation for cis- and trans-1,2-cyclohexanediol was significantly larger than for trans-2-methoxycyclohexanol, the reverse is true for the disproportionation rate constants. The net result is that the overall rate constants, kK, are about the same for these compounds. Johnson (69) has suggested that the relative magnitudes of equilibrium constants and disproportionation rate constants may be related to the stability of the intermediate complexes and the geometries of the resulting transition states.

The theory assumes that 1,2-glycols are oxidized via chelate intermediate complexes and that the α-methoxyalcohol is oxidized by a less stable complex. Consider the reactions and free energy diagrams given in Fig. 13. Figure 13A shows the hypothetical reaction of a diol in which the energy minimum for complex formation, chelate stabilization, is pronounced and indicative of a large equilibrium constant for complex formation. The free energy of activation, ΔF_A, required to promote the excitation of the complex to the transition state is conceivably rather large, which would predict a relatively low disproportionation rate constant. For the α-methoxyalcohol, Fig. 13B shows the case in which the intermediate complex is not particularly stable, as indicated by the relatively high free energy state for the complex. Assuming that the free energy

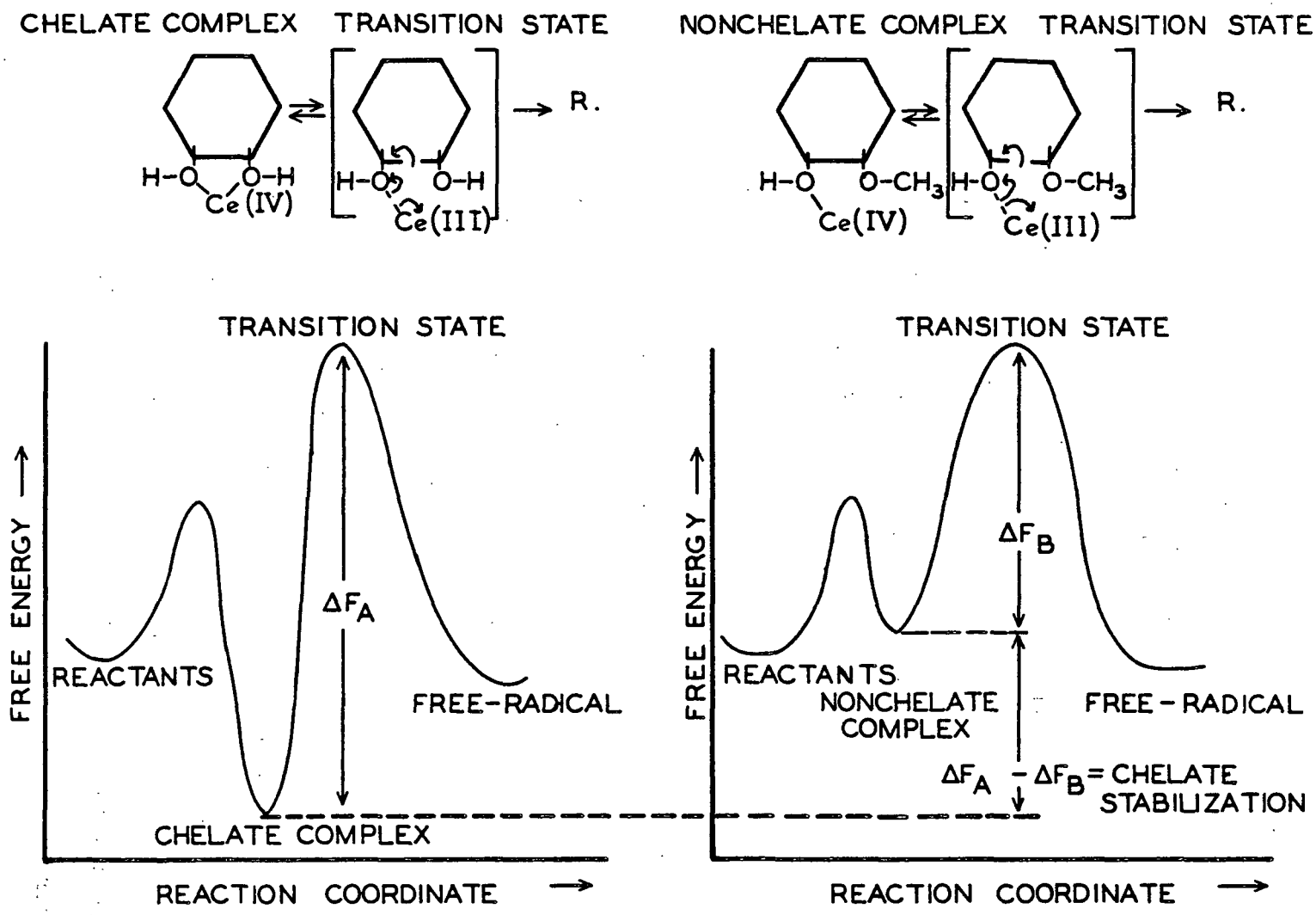


Figure 13A

Figure 13B

Figure 13. Transition State Energy Diagrams for Reactions with Chelated and Nonchelated Intermediate Complexes. (Examples: the Cerium(IV) Oxidations of Diols and Diol Monomethyl Ethers)

maximums corresponding to the activated complexes (transition states) for both reactions (Fig. 13A and 13B) are nearly equal, probably a good assumption since the transition state geometries are potentially similar, then it is seen that the activation free energy, ΔF_B for the excitation of the α-methoxyalcohol complex is less than ΔF_A for the diol and predicts a higher disproportionation rate constant for the acyclic complex. The experimental results seem to be consistent with this theoretical explanation.

MECHANISM OF GLUCOSE OXIDATION BY CERIUM(IV)

As described in previous sections, glucose is oxidized by cerium(IV) in perchloric acid to produce arabinose, formic acid, and cerium(III). The kinetics of this reaction were studied and showed that glucose and cerium(IV) interact in an equilibrium step to form an intermediate complex which is assumed to disproportionate forming a free radical and reduced cerium(III). The free radical is then further oxidized in a rapid second attack by cerium(IV) to form the product and a second mole of cerium(III).

The nature of the intermediate complex as deduced from the magnitude of the equilibrium constant, (Table VIII), and the reactivity of 2-deoxy-D-glucose, (Table IX), is believed to involve both the C_1 and C_2 hydroxyls in a chelate complex. In Fig. 14 is depicted the reaction mechanism described above which explains the products and kinetics of glucose oxidation by cerium(IV). It is to be noted that the formation of formate esters has been established in periodate and lead tetraacetate oxidations of glucose (61). The formation of the formate ester may not occur in ceric oxidations, but is postulated by analogy to the above cases. It is assumed that formate esters are rapidly hydrolyzed in 1.0M perchloric acid. However, if formate esters are not rapidly hydrolyzed under these conditions, then an alternate mechanism which produces arabinose and formic acid directly is

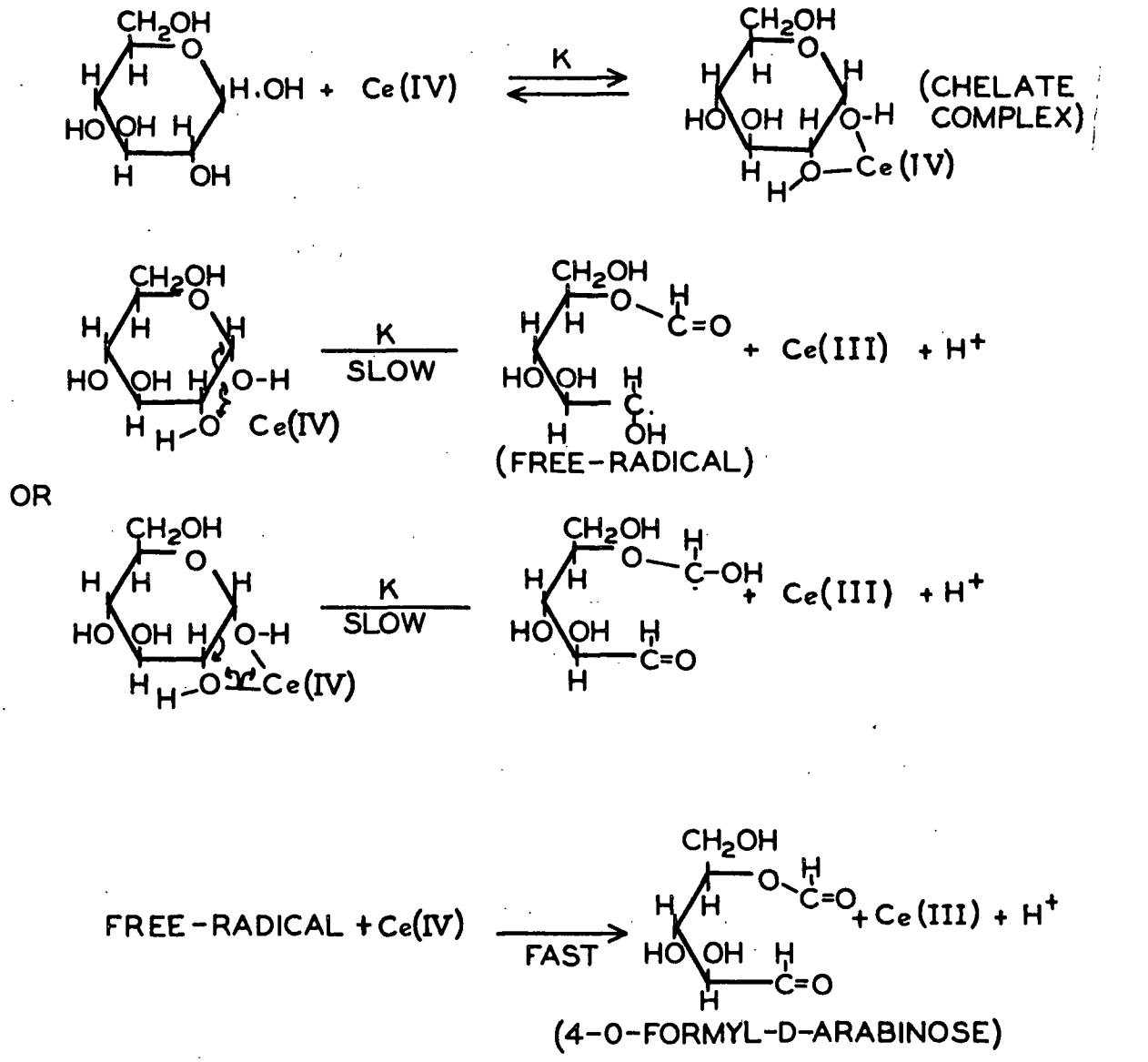


Figure 14. Mechanism of Glucose Oxidation by Cerium(IV) in 1.0M Perchloric Acid

required to explain the data. Such a mechanism is possible, involving the free aldehyde form of the reducing sugar, and is presented in Fig. 15. Studies of cerium(IV) oxidations of ribose, which has about 10% free aldehyde in aqueous solution (70) as compared to 0.012% for glucose showed no significant increase in rate, (Table IX), so it seems probable that the mechanism involves the pyranose form of aldoses.

In Fig. 14 the mechanism is depicted in two ways since it is not known whether the location of the free-radical is determined by factors affecting radical stability or whether the position of the radical is simply the result of chance.

MECHANISM OF ANHYDRO-D-GLUCOSE OXIDATION BY CERIUM(IV)

The products and kinetics of reactions of Schardinger β-dextrin (anhydro-D-glucose) and cellulose indicate that the known facts may be rationalized by the mechanism shown in Fig. 16. The hydroxyl groups at C_2 and C_3 of an anhydro-D-glucose unit form a chelate complex with cerium(IV). The complex disproportionates forming a free radical which is rapidly oxidized by a second mole of cerium(IV).

TEMPERATURE DEPENDENCE FOR OXIDATIONS BY CERIUM(IV)

The temperature dependence for cerium(IV) oxidation of glucose, methyl β-D-glucopyranoside, 1,5-anhydro-D-glucitol and Schardinger β-dextrin was determined by studies at 10, 15, and 20°C., respectively. All compounds exhibited Arrhenius temperature dependence, Fig. 17. The calculated activation energies, activation enthalpies, and activation entropies are given in Table XI.

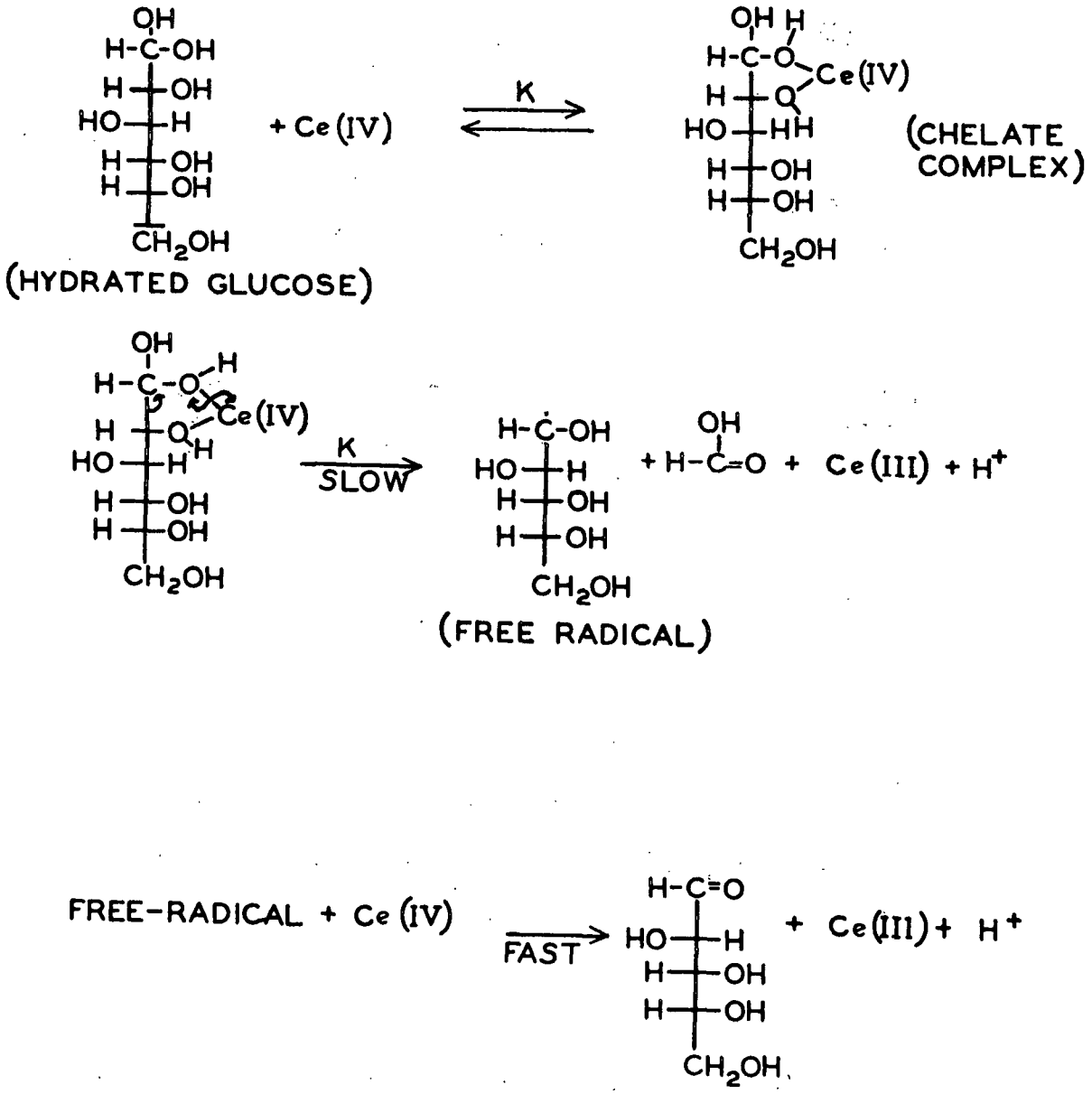
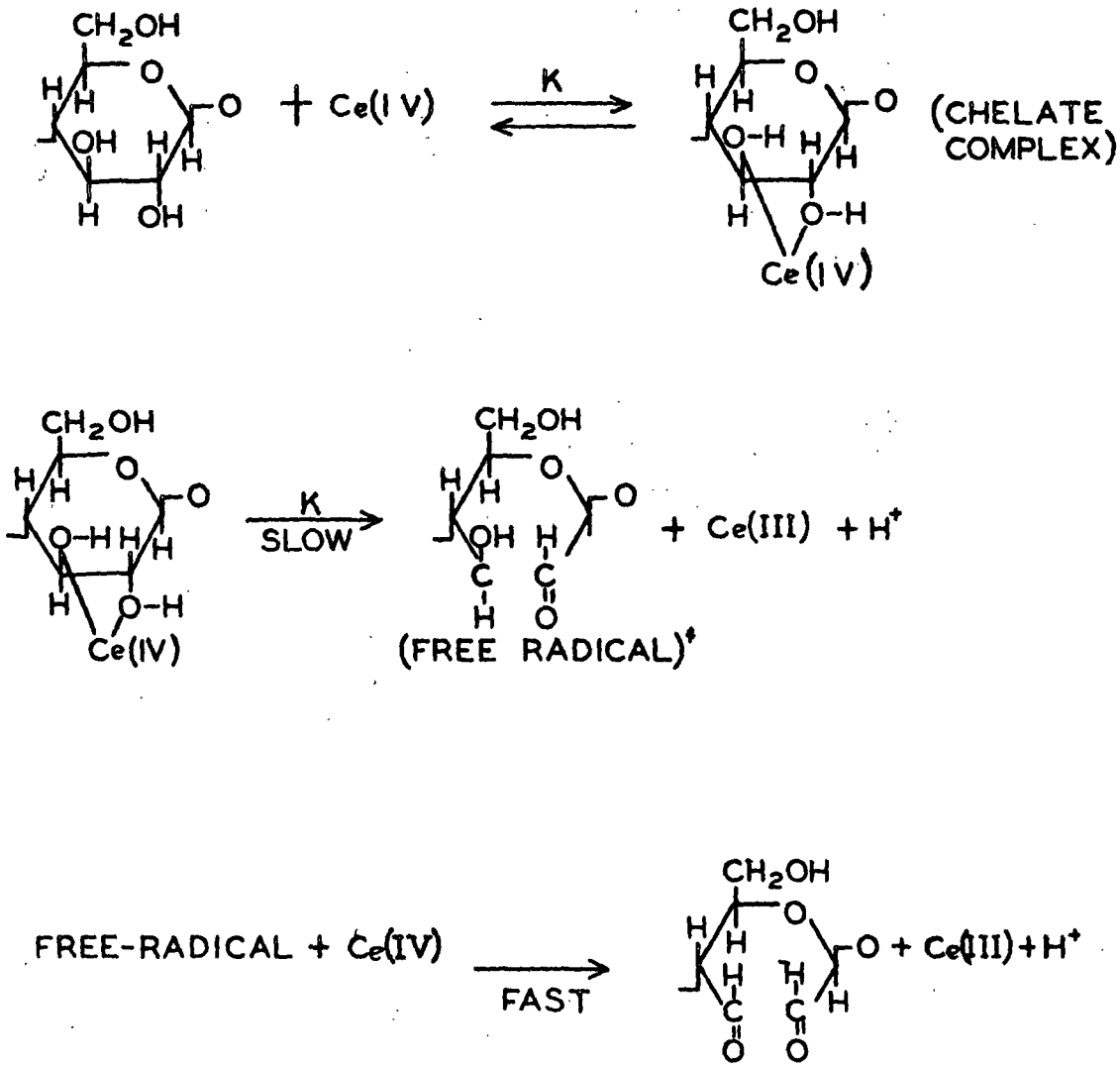
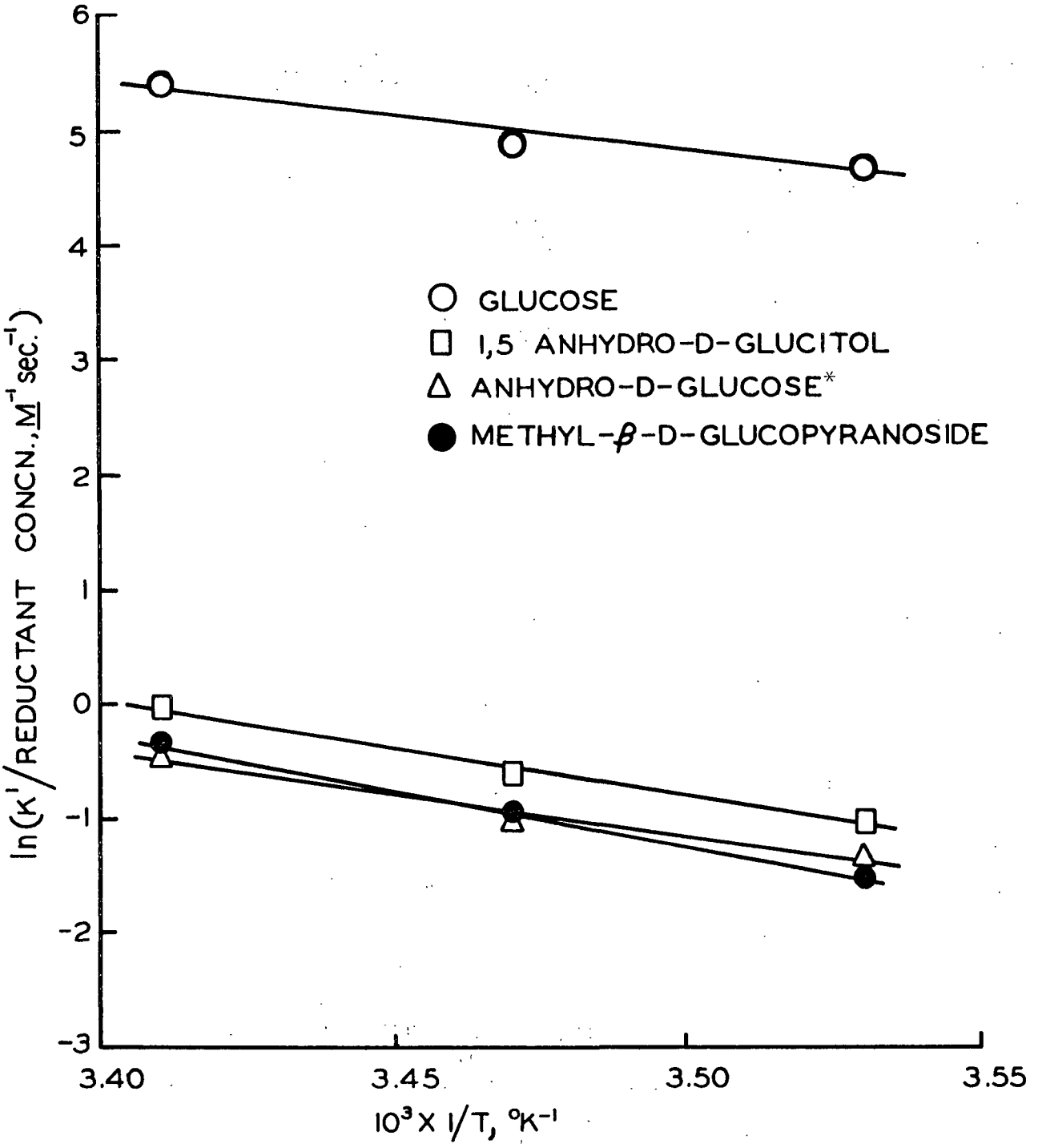


Figure 15. Open Chain Oxidation of Glucose by Cerium(IV)



*FREE-RADICAL MAY EXIST AT EITHER THE C_2 OR C_3 POSITIONS.

Figure 16. Mechanism of Anhydro-D-Glucose Unit Oxidation by Cerium(IV) in 1.0M Perchloric Acid



*Schardinger β-dextrin.

Figure 17. Arrhenius Plots for Reactions in 1.0M Perchloric Acid

TABLE XI

THERMODYNAMIC DATA FOR CERIUM(IV) REACTIONS
IN 1.0M PERCHLORIC ACID

Compound	E_a, kcal. mole^{-1}	$\Delta H + \Delta H^{\ddagger}$, kcal. mole^{-1}	$\Delta S + \Delta S^{\ddagger}$, E.U.
Cyclohexanol[a]	24.8	24.2	15.4
cis-1,2-Cyclohexanediol[a]	26.1	25.5	27.5
trans-1,2-Cyclohexanediol[a]	27.1	26.5	28.7
trans-2-Methoxycyclohexanol[a]	27.6	27.0	31.0
1,5-Anhydro-D-glucitol	17.3	16.7	-9.5
Methyl β-D-glucoside	19.6	19.0	-2.4
Anhydro-D-glucose[b]	13.7	13.2	-22.7
Glucose	13.6	13.0	-11.5

[a]Data from reference (5).
[b]Schardinger β-dextrin.

Bunnett (71) discusses the temperature dependence of complex reactions of the type

$$A + B \underset{}{\overset{K}{\rightleftharpoons}} C \xrightarrow{k} D$$

in which the first step is rapidly reversible with equilibrium constant K and the second step, with rate constant k, is rate controlling. In this case the overall rate constant is the product of k times K or kK. From thermodynamics

$$K = \exp(-\Delta H/RT)\exp(\Delta S/R) \qquad (23)$$

and from transition state theory

$$k = (k_B T/h)\exp(-\Delta H^{\ddagger}/RT)\exp(\Delta S^{\ddagger}/R) \qquad (24).$$

Combining to get the product, kK

$$kK = (k_B T/h)\exp[-\Delta H+\Delta H^{\ddagger})/RT]\exp[(\Delta S+\Delta S^{\ddagger})/R] \qquad (25)$$

which means that the overall rate constant kK exhibits the same type of temperature

dependence as a specific rate constant except that the calculated enthalpy and entropy of activation are actually the sums of the equilibrium and rate-controlling steps. Under these circumstances no mechanistic interpretation of activation data should be made since the relative contributions from the equilibrium step and from the rate-determining step are uncertain without further information (see Appendix).

OXIDATIONS OF CELLULOSE MODEL COMPOUNDS

In the Introduction it was pointed out that most authors have suggested that cellulose oxidation by cerium(IV) involves reaction at the C_2-C_3 diol group or at the C_6 hydroxyl of an anhydro-D-glucose unit. Hintz (5) compared the relative rates of oxidation of trans-1,2-cyclohexanediol, cyclohexanemethanol, and tetrahydropyran-2-methanol as models for the C_2-C_3 glycol and C_6-hydroxyl groups and predicted that the diol group of cellulose would be oxidized about six times faster than the C_6 hydroxyl.

The results of this study show that, using carbohydrate compounds as models for cellulose, the reducing function is 360 times more reactive than an anhydro-D-glucose repeating group (Table IX). Furthermore, no evidence was obtained which indicated reaction of the C_6 hydroxyl under the conditions used.

Product analysis studies with the kinetic model for anhydro-D-glucose, Schardinger β-dextrin, and with authentic cellulose showed the presence of erythrose and glyoxal in hydrolyzates of the oxidized polysaccharides. This evidence suggests preferential cleavage of the C_2-C_3 bonds of anhydro-D-glucose as was originally expected.

Based on the results of this study it seems reasonable to predict that cellulose oxidation takes place predominantly at either the C_2-C_3 diol or at

the reducing end-group. The relative importance of oxidations at the two sites will depend to a great extent on degree of polymerization and accessibility of reducing end-groups.

CONCLUSIONS

Cerium(IV) oxidations of glucose, anhydro-D-glucose, 1,5-anhydro-D-glucitol, and methyl β-D-glucopyranoside proceed via chelate intermediate complexes, as indicated by the magnitude of the equilibrium constants determined by kinetic and spectrometric techniques. Further evidence, obtained from studies of C_1-C_2 substituted glucose derivatives, indicates that glucose oxidation by cerium(IV) involves the preferential coordination of the oxidant with the C_1 hydroxyl and an interaction with the oxygen of the C_2 substituent. The effect of 2-O-methyl substitution on glucose was an increase in overall rate of oxidation. Thus, either 2-O-methyl glucose and glucose, which yield the same reaction product, are oxidized by similar chelate intermediate complexes, or the similarity of the geometries of the transition states for the glucose chelate and the acyclic 2-O-methyl-D-glucose intermediate combined with compensating differences in complex stability and disproportionation rate constants leads to nearly identical overall rates.

Oxidation of excess glucose by cerium(IV) in 1.0M perchloric acid gives a quantitative yield of arabinose and formic acid. This controllable degradation of reducing sugars may have synthetic application.

Consideration of the relative rates of oxidation of the cellulose model compounds used in this study suggests that the reducing end-group is 360 times more reactive than the anhydro-D-glucose repeating unit or the nonreducing end-group. Assuming equal accessibility in a cellulose of normal degree of polymerization (D.P.), the high relative concentration of anhydro-D-glucose units predicts that most oxidative attacks will involve cleavage of a C_2-C_3 bond. However, for low D.P. celluloses, oligomers, or samples in which end-groups are more accessible, the reactivity of the reducing-end group will predominate and attack will occur primarily by C_1-C_2 cleavage.

EXPERIMENTAL PROCEDURES

PREPARATION AND PURIFICATION OF COMPOUNDS

Compounds which are commercially available were purchased and purified by appropriate techniques. Other compounds were synthesized using procedures described in the literature. Melting points were determined with a "Uni Melt"* apparatus and are uncorrected. Melting points, optical rotation and in some cases infrared spectra were used to identify the compounds used in this study.

SOURCE OF ORGANIC COMPOUNDS

D-GLUCOSE

Anhydrous dextrose, Mallinckrodt Chemical Works, analytical reagent was used without further purification. Paper chromatography of this material showed no detectable impurities. The melting point was 144.5-146°C. [lit. m.p. 146°C. (72)].

METHYL β-D-GLUCOPYRANOSIDE

Methyl β-D-glucopyranoside was purchased from Pfanstiehl Laboratories. The glucoside was purified by digesting 20 min. at 80°C. in 1.0M sodium hydroxide to degrade any glucose present to saccharinic acids. The solution containing methyl β-D-glucopyranoside and saccharinic acids was deionized on a column of Amberlite MB-3 (Rohm and Haas) mixed anion-cation exchange resin. The methyl β-D-glucopyranoside was crystallized from methanol, m.p. 108-110°C.; $[\alpha]_D^{20}$ -33.23°(c, 1.39 water)[lit. m.p. 109-111°C.; $[\alpha]_D^{20}$ -32.5°(c, 1.0 water (73)].

*Arthur H. Thomas Co., Philadelphia, Pa.

SCHARDINGER β-DEXTRIN (ANHYDRO-D-GLUCOSE)

Schardinger β-dextrin was purchased from Pierce Chemical Co. The analysis supplied by the manufacturer is as follows:

Appearance	white crystalline solid with varying degrees of hydration
Appearance (1% aqueous solution)	clear and colorless
Specific rotation $[\alpha]_D^{20}$	+ 140° (c, 1.0 water) concentration not corrected for hydration.

The Schardinger β-dextrin was found to be nonreducing to Fehling solution and produced only glucose when degraded by mild acid hydrolysis. A sample dried in a vacuum oven at 80°C. for 6 hr. gave a specific rotation, $[\alpha]_D^{20}$ + 157.4° (c, 1.2 water). Literature values for specific rotation are $[\alpha]_D$ + 158 (c, 1 water) (74) and $[\alpha]_D$ + 162.5 (c, 1 water) (75). For the purpose of this research the compound was considered to be pure anhydro-D-glucose units.

CELLULOSE

Whatman Standard Grade cellulose powder was used without further purification.

1,5-ANHYDRO-D-GLUCITOL

1,5-Anhydro-D-glucitol was prepared by the lithium aluminum hydride reduction of 2,3,4,6-tetraacetyl-glucosyl-bromide as described by Ness, Fletcher, and Hudson (76). The preparation was freed of glucose by digestion with 1.0M sodium hydroxide as described for the purification of methyl β-D-glucopyranoside. The compound was crystallized from hot absolute ethanol and recrystallized from hot methanol, m.p. 138-139°C. (lit. 142-143°C.). The specific rotation was

$[\alpha]_D$ -42.6 (c, 2.14 water) [lit. $[\alpha]_D$ - 42.8 (c, 2.14 water) (76)]. Paper chromatographic analysis showed only pure 1,5-anhydro-D-glucitol.

2-O-METHYL-D-GLUCOSE

A sample of 2-O-methyl-D-glucose was obtained from Dr. Seib (77). It had been prepared by the diazomethane methylation of 1,3,4,6-tetra-O-acetyl-α-D-glucopyranose. The 1,3,4,6-tetra-O-acetyl-α-D-glucopyranose was prepared by the procedure of Helferich and Zirner (78). Methylation of 1,3,4,6-tetra-O-acetyl-α-D-glucopyranose was by the method of Mastronardi, et al. (79). The resulting 2-O-methyl-1,3,4,6-tetra-O-acetyl-α-D-glucose was crystallized from ethanol, m.p. 106-107°C. [lit. m.p. 107-108°C. (79)]. The compound was deacetylated using 1N sodium methoxide in dry methanol (77) yielding 2-O-methyl-β-D-glucose which on recrystallization from hot absolute ethanol gave crystals, m.p. 156-157°C. [lit. m.p. 160°C. (80)]. No impurities were detected in this compound when analyzed by thin-layer chromatography using silica gel G. plates in ethyl acetate:methanol (9:1).

METHYL β-D-GALACTOPYRANOSIDE

A sample of methyl β-D-galactopyranoside, m.p. 176-177°C. and specific rotation $[\alpha]_D^{30}$ 0° (water), which was prepared by Gasman (81) was used in this study [lit. m.p. 178-179°C.; $[\alpha]_D$ -0.61° (water) (82)].

2-O-METHYL-D-GALACTOSE

A sample of 2-O-methyl-D-galactose, m.p. 150-151°C. and specific rotation $[\alpha]_D^{25}$ +86° (c, 0.816 water), which was prepared by Gasman (81) was used in this study [lit. m.p. 145-148°C. $[\alpha]_D^{18}$ +94° (c, 0.5 water) (83)].

METHYL-2,3,4,6-TETRA-O-METHYL-β-D-GLUCOPYRANOSIDE

Methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside was prepared by methylation of methyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside using the procedure of Falconer and Adams (84). The product was distilled in a Nester-Faust spinning band still. The methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside crystallized in the receiver, m.p. 38.5-40°C., $[\alpha]_D$ -17.3° (c, 12.0, 1.0N perchloric acid) [lit. m.p. 40-41°C., $[\alpha]_D^{20}$ -17.3 (c, 4.4 water) (85)].

METHYL-4,6-DI-O-METHYL-β-D-GLUCOPYRANOSIDE

A sample of methyl-4,6-di-O-methyl-β-D-glucopyranoside prepared by Bayer (86) was used in this study. This compound had m.p. 75-76° with specific rotation $[\alpha]_D^{18}$ -29.9 (c, 1.7 chloroform) [lit. m.p. 77-79 with $[\alpha]_D^{18}$ -28.8 (c, 3 chloroform) (85)].

2,3,4,6-TETRA-O-METHYL-D-GLUCOSE

A sample of 2,3,4,6-tetra-O-methyl-D-glucose which was prepared by Hintz (87) was used in this study. Methyl-2,3,4,6-tetra-O-methyl-D-glucopyranoside was prepared by the procedure of Walker, et al. (88) and hydrolyzed to give 2,3,4,6-tetra-O-methyl-D-glucose. This compound had m.p. 85-86°C. [lit. m.p. 96°C. for 2,3,4,6-tetra-O-methyl-α-D-glucose (89)]. Gas chromatography as the trimethylsilyl ether derivative by the method of Sweeley, et al. (90) showed only two peaks, assumed to be the α- and β-anomers.

2-DEOXY-D-GLUCOSE

2-Deoxy-D-glucose was purchased from Pfanstiehl Laboratories and used without further purification, m.p. 145-146°C. [lit. m.p. 142-144°C. (91)].

CELLOBIOSE

Cellobiose, Eastman Organic Chemicals, was used without further purification.

D-RIBOSE

D-Ribose was purchased from Pfanstiehl Laboratories and used without further purification.

D-GALACTOSE

D-Galactose was purchased from Matheson Coleman and Bell and used without further purification.

ERYTHROSE

A sample of erythrose was purchased from K and K Laboratories and used as a chromatographic reference without further purification.

ERYTHRITOL

A sample of erythritol was purchased from Pierce Chemical Company and used without further purification.

PREPARATION OF SOLUTIONS FOR OXIDATION REACTIONS

REACTION MEDIA

Cerium(IV) oxidations of organic reductants were conducted in either 1.0M perchloric acid or in a solution of 0.25M sulfuric and 0.75M perchloric acids. Stock solutions of these acids (2.0M) were prepared from reagent-grade concentrated sulfuric acid and 70% perchloric acid. The stock solutions were standardized with a sodium hydroxide solution which had been standardized with primary standard

potassium acid phthalate. Reaction media were prepared by appropriate dilution of the stock solutions. The 1.0M perchloric acid solutions used as reaction media for most reactions conducted was restandardized with standard sodium hydroxide before use. Ordinary distilled water was redistilled from alkaline potassium permanganate and dilute sulfuric acid for use in preparation of all solutions.

CERIUM(IV) SOLUTIONS

A stock solution of 0.05M cerium(IV) in 1.0M perchloric acid was prepared by appropriate dilution of a commercial ceric perchlorate solution purchased from G. Frederick Smith Chemical Co. The exact cerium(IV) and acid concentrations of the commercial reagent were determined by the procedure of Offner (24). The concentrations of cerium(IV) solutions were determined by titration of weighed samples of primary standard arsenic trioxide using osmium tetroxide as a catalyst and 1,10(ortho)-phenanthroline as the indicator (92).

A stock solution, 0.05M cerium(IV) in 0.25M sulfuric and 0.75M perchloric acid, was prepared by dissolving ceric sulfate (G. Frederick Smith Chemical Co.) in this acid solution. This solution was used for reactions in sulfate-containing media.

SOLUTIONS OF ORGANIC SUBSTRATES

The carbohydrate solutions used in kinetic experiments were prepared by dissolving weighed amounts of the pure compounds in 1.0M perchloric acid or in mixed 0.25M sulfuric and 0.75M perchloric acids, to give the required concentration.

Hygroscopic compounds were dried in a vacuum oven to constant weight before preparing solutions for kinetics in order to minimize errors due to weighing.

STABILITY OF GLYCOSIDIC BOND IN REACTION MEDIUM

Determinations of the rate of hydrolysis of methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside in 1.0M perchloric acid and in a solution of 0.04M cerium(III) in 1.0M perchloric acid were made at room temperature. This compound was chosen to demonstrate glycosidic bond stability in the reaction medium, since it has been shown (93) that the β-anomer is hydrolyzed more rapidly than the α-form and that increased methyl substitution on methyl glucosides increases the rate of hydrolysis (85).

The reaction mixtures were prepared by dissolving a known amount of glucoside in a given volume of perchloric acid solvent. The rate of hydrolysis was followed polarimetrically. Table XII shows that no significant hydrolysis occurs under the conditions used for kinetic studies in this research.

TABLE XII

RESULTS OF ROOM TEMPERATURE HYDROLYSIS OF METHYL-2,3,4,6-TETRA-O-METHYL-β-D-GLUCOPYRANOSIDE[a]

Experiment	Specific Rotation, $[\alpha]_D$		Total Reaction Time, hr.
	initial	final	
A	-17.3°	-17.3°	158.6
B	-17.14°	-17.31°	158.6

A = Methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside in 1.0M perchloric acid.
B = Methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside in 0.04M cerium(III) and 1.0M perchloric acid.

[a] $[\alpha]_D$ (c, 12.3 in solvent described for each experiment). Temperature range 18-24°C.

Further evidence supporting the stability of the glycosidic bond under the conditions used in this work was obtained by proving that no hydrolysis product, 2,3,4,6-tetra-O-methyl-D-glucose, was present in the solutions after 158.6 hr.

The samples were deionized and treated by the trimethylsilation procedure of Sweeley, et al. (90). Gas chromatography of these samples (column, 30% DEGS on 60/80 mesh acid-washed Chromosorb W; temperature 170°C.; carrier gas, helium) showed that only methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside was present. These experimental results are in agreement with the finding of Dyfverman (94) who demonstrated that methyl β-cellobioside was stable to 2.0M hydrochloric acid for at least 16 days at room temperature.

PRODUCT ANALYSIS PROCEDURES

CERIUM(IV) OXIDATIONS FOR PRODUCT ANALYSIS

In all oxidations for product analysis the reductant concentration was maintained in at least a twofold excess on a mole basis. All reactions in 1.0M perchloric acid were conducted in vessels immersed in a constant temperature bath and reactants were purged for 30 min. with prepurified nitrogen to minimize dissolved oxygen concentration.

PAPER CHROMATOGRAPHY

Qualitative identification of reaction products from cerium(IV) oxidations of various reductants were made by comparative descending paper chromatography. Compounds were identified by comparing their mobilities in two developers with those of known compounds. These chromatograms were run on Whatman No. 1 paper exclusively.

The two developers used in this work were; (1) Ethyl acetate:pyridine:water (8:2:1 V/V); and (2) ethyl acetate:acetic acid:formic acid:water (18:3:1:4 V/V).

The following reagents were used to detect compounds on the developed chromatograms:

(1) Silver nitrate-sodium hydroxide-sodium thiosulfate (95)

(2) p-Anisidine hydrochloride (96)

(3) Urea phosphate (97)

Reagent (1), which was employed as a three-stage dip, detected a wide variety of compounds. Reagent (2), which was applied as a spray followed by heating at 105°C. for short times, was useful in determining reducing sugars and in differentiating between aldohexoses and aldopentoses. Reagent (3), which was applied as a spray followed by heating at 105°C. for short times, was useful in detecting ketoses.

Preparative paper chromatography was used to separate reaction products from unreacted starting materials. Whatman 3MM papers were prewashed with 50% ethanol-water and dried. The sample was applied along a line perpendicular to the cross-machine direction of the paper and known compounds were spotted on guide zones near the edges of the sheet. After development, the guide strips were removed and detected using silver nitrate-sodium hydroxide-sodium thiosulfate. Using the guide strips as a reference the appropriate areas of the chromatogram were excised and the individual compounds were eluted from the paper with distilled water.

DETERMINATION OF REACTION PRODUCTS

GLUCOSE

The stoichiometry of glucose oxidation by cerium(IV) was established by determining the yield of arabinose. The method used to establish the yield of product involved the oxidation of 5.55×10^{-3} moles of glucose by 2.775×10^{-3} moles of cerium(IV) in 1.0M perchloric acid at 20°C. The reaction mixture was neutralized with potassium hydroxide and deionized using Amberlite MB-3 mixed

cation-anion exchange resin. After concentration the neutral solution containing arabinose and glucose was submitted* for quantitative analysis by the method of Saeman, et al. (65).

A small sample of arabinose was isolated from a glucose-cerium(IV) oxidation mixture by preparative paper chromatography. Using the procedure of Zinner (98) the arabinose diethyldithioacetal, m.p. 124-125°, mixed m.p. 124-125°C. was obtained [lit. m.p. 125-125.5°C. (98)]. The infrared spectrum of the material prepared from arabinose isolated from a cerium(IV)-glucose oxidation mixture was identical to that of arabinose-diethydithioacetal prepared from authentic arabinose.

The qualitative identification of formic acid as a product of cerium(IV) oxidation of glucose was made by analyzing the distillate from a reaction mixture by the method of Feigl (66). The distillate was obtained by collecting the condensate during the room-temperature, low-pressure evaporation of a cerium(IV)-glucose reaction mixture.

ANHYDRO-D-GLUCOSE

Determination of products from reactions of Schardinger β-dextrin or cellulose required that the oxidized polysaccharide be completely hydrolyzed before analysis was made.

Before hydrolysis the oxidized polysaccharide was removed from the reaction media. Oxidized Schardinger β-dextrin was found to form an insoluble complex with xylene. Isolation was achieved by addition of several milliliters of xylene followed by vigorous shaking and subsequent collection of the resulting

*Analytical Department, The Institute of Paper Chemistry, Appleton, Wisconsin.

precipitate. The precipitate was washed with water to remove all perchloric acid and then suspended in water. The suspension was heated on a steam bath until a clear solution developed; this treatment drives off the xylene destroying the complex.

Cellulose, which is insoluble in the reaction media, was simply filtered and washed to free it of perchloric acid after oxidation.

The oxidized Schardinger β-dextrin was hydrolyzed by refluxing in approximately 0.7N sulfuric acid for 2 hr. The hydrolyzate was then neutralized with sodium hydroxide to pH 5 and concentrated for spotting on paper chromatograms.

Oxidized cellulose was hydrolyzed by dissolving in 72% sulfuric acid and then diluting to 9% sulfuric acid and refluxing for 4 hr.

A more complicated hydrolysis procedure was employed when studying oxidized cellulose in an attempt to establish reaction stoichiometry of the cerium(IV)-anhydro-D-glucose reaction. It has been shown (99) that the hydrolysis of periodate-oxidized starch is facilitated by the use of sulfur dioxide. In the hydrolysis of oxidized cellulose the sample was dissolved in 10 ml. 72% sulfuric acid; after 20 min. a solution of 17.5 g. sulfur dioxide in 125 ml. ice-water was added to the oxidized cellulose solution in a Teflon-lined Parr Bomb* (100). The bomb was sealed and placed in an oven at 115°C. After 7 hr. the bomb was removed from the oven and cooled. The sulfur dioxide was removed by low pressure evaporation and the solution was deionized by passing it through a column of Amberlite MB-3 mixed anion-cation exchange resin. The deionized hydrolyzate was concentrated and used to spot preparative paper chromatograms.

*Parr Instrument Co. 211 53rd Street, Moline, Illinois.

Hydrolysis of an unoxidized sample of Whatman Standard Grade cellulose by the above procedure followed by qualitative paper chromatographic analysis showed that fructose was produced under these conditions.

Paper chromatography of the hydrolyzates of oxidized Schardinger β-dextrin and oxidized cellulose showed that the product was erythrose in both cases. Quantitative determination of the amount of erythrose recovered from the hydrolyzate of a cerium(IV) oxidized cellulose was accomplished using the method of Smith and Duke (68). The hydrolyzate was separated by paper chromatography permitting isolation of glucose, fructose, and erythrose. The amounts of each sugar were determined by quantitative oxidation by excess cerium(IV).

The identity of erythrose as a product obtained from hydrolysis of cerium(IV)-oxidized anhydro-D-glucose was shown by comparative paper chromatography in two developers and by gas chromatographic experiments. Known samples of erythrose and erythritol were treated by the procedure of Sweeley, et al. (90) to form the trimethylsilyl ether (TMS) derivatives. These were easily resolved by gas chromatography on an SE-30 column at 135°C. Further experiments with the TMS-erythrose using the hydrolysis procedure of Reist and Holton (101) and the reduction procedure of Crowell and Burnett (102) showed that it was possible to remove the TMS groups, reduce the erythrose to erythritol, and finally to form the TMS-erythritol. This reaction scheme is depicted below.

$$\text{TMS-Erythrose} \xrightarrow[\text{20 hr.}]{\text{50\% aqueous methanol}} \text{Erythrose} \xrightarrow[\text{Water}]{NaBH_4} \text{Erythritol} \longrightarrow \text{TMS-Erythritol}$$

A sample of erythrose isolated from the hydrolyzate of cerium(IV) oxidized cellulose was analyzed by the above series of reactions, and positive evidence for TMS-erythrose and TMS-erythritol was obtained.

Glyoxal was qualitatively identified in hydrolyzates of cerium(IV)-oxidized cellulose and Schardinger β-dextrin by adding 10 ml. of hydrolyzate to 40 ml. 2N hydrochloric acid saturated with 2,4-dinitrophenylhydrazine. The precipitated 2,4-dinitrophenylhydrazones were analyzed by comparative thin-layer chromatography on silica gel G. In two developers, benzene:tetrahydrofuran (93:7) and benzene:-petroleum ether* (3:1), the product 2,4-dinitrophenylhydrazones were identical to the derivatives of known glyoxal.

KINETIC MEASUREMENTS

All kinetic experiments were conducted with the organic reductant in excess over the cerium(IV), on a mole basis, so that reactions would be pseudo-first-order. Under these conditions the possibility of complications due to secondary oxidation of primary products is reduced. Furthermore, the participation of intermediate complexes and the equilibrium constant for their formation can be determined by varying the excess of organic reductant (provided the equilibrium constant is sufficiently large).

Most kinetic runs were run in duplicate. The results of the individual kinetic runs are tabulated in Appendix I.

REMOVAL OF DISSOLVED OXYGEN

Hintz (5) found that the presence of dissolved oxygen in the reaction media led to autocatalytic behavior in the cerium(IV) oxidations of cyclohexanediols in 1.0M perchloric acid. This autocatalytic behavior was minimized by purging the reactants with nitrogen before mixing. To prevent possible

*Petroleum ether boiling range (60-110°C.).

interference by oxygen, all reactant solutions used in this study were purged 30 min. with prepurified nitrogen before initiation of the reaction.

TEMPERATURE CONTROL

The reaction temperature was controlled by use of a thermostatted water bath and was monitored by use of a pair of matched precision thermometers. The thermometers were calibrated by comparing with a National Bureau of Standards thermometer.

The temperature of the reaction mixture was maintained by circulating water from the constant-temperature bath through a special cell holder (Cary No. 1540750) and through the walls of the cell compartment of the Cary Model 15 spectrophotometer. The reaction temperatures reported are the mean of the temperatures measured at the inlet and outlet of the cell jacket. Temperature fluctuations were less than 0.03°C. at the inlet and outlet measurement stations.

For rapid reactions requiring the use of a direct injection technique, a thermostatted syringe jacket was designed which effectively controlled the temperature of the syringe and its contents before injection into the cell.

SPECTROMETRIC RATE DETERMINATIONS

Hintz (5) and Ardon (16) have demonstrated that cerium(IV) reaction rates determined titrimetrically agree with rates determined spectrometrically. The spectrometric method of rate determination is based on the fact that the absorbance of cerium(IV) solutions is directly proportional to the cerium(IV) concentration. The adherence to Beers Law has been demonstrated (5) for the cerium(IV) concentration range used in this work and the spectrophotometer was shown to be linear over the range from 0 to 2 absorbance.

Reaction mixtures for normal or relatively slow reactions, k' less than 10^{-2} sec.$^{-1}$, were prepared by the technique described by Hintz (5). Appropriate amounts of cerium(IV) solution in the desired acid medium were placed in an ampule made by blowing thin one end of a 20-cm. length of 12-mm. glass tubing. The ampule was placed in a 19 x 3 cm. test tube containing the required amount of organic reductant in aqueous acid solution. The test tube was placed in a constant temperature bath, and both reactant solutions were purged for 30 min. with prepurified nitrogen. The reaction was initiated by breaking the ampule and mixing the reactants. A sample of the reaction mixture was then transferred to the cell in the spectrophotometer. At the moment of breaking the ampule a stopwatch was started so that the time lag between initiation and first recording of absorbance was known.

For reactions which were relatively fast, k' greater than 10^{-2} sec.$^{-1}$, the reactants were mixed within the spectrophotometer cell. The required amount of oxygen-free oxidant solution, up to 0.25 ml. of 0.05M cerium(IV) in 1.0M perchloric acid was placed in the spectrophotometer cell; then a 1.5-mm. inside diameter glass tube, bent as shown in Fig. 18, was placed in the spectrophotometer cell in the cell holder. The syringe, filled with the desired amount of oxygen-free substrate solution, up to 2.75 ml. plus an amount equal to the volume of connecting tubing, was placed within the syringe temperature control jacket and allowed to equilibrate for 30 min. In practice all reactant solutions and equipment were maintained at reaction temperature by means of the constant temperature bath. Reactions were initiated by depressing the syringe plunger with the spectrophotometer in operation. Thus, recording of data was begun with a time lapse of approximately 1 second.

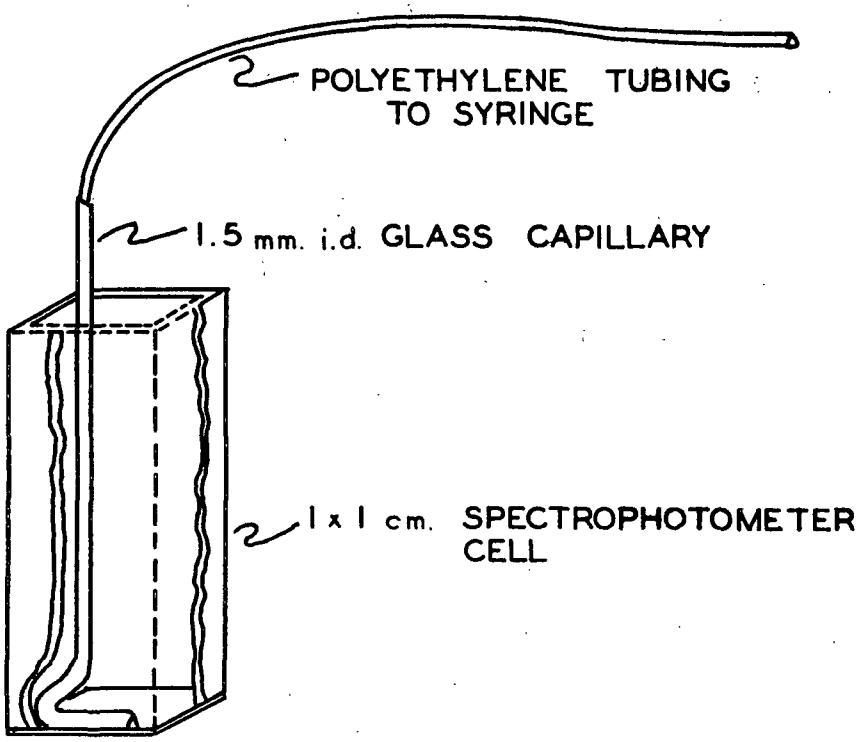


Figure 18. Schematic View of Mixing Tube Used for Kinetic Studies of Rapid Reactions in the Cary Recording Spectrophotometer

PRECISION OF KINETIC MEASUREMENTS

Reactions with rate constants lower than 10^{-2} sec.$^{-1}$ were carried out using the technique devised by Hintz (5) and described in the preceding section. Table XIII shows the results of duplicate experiments obtained by this method. All determinations of rates involving methyl β-D-glucopyranoside used in determining equilibrium constants for complex formation and disproportionation rate constants were run in duplicate (see Appendix I, Table XIV). Reactions of 1,5-anhydro-D-glucitol and Schardinger β-dextrin were not duplicated in most cases. The poorest reproducibility observed was in duplicate determinations of the rates of cerium(IV) oxidations of 2-deoxy-D-glucose at 15°C. and Schardinger β-dextrin at 10°C. where the deviations from the mean were 10%. In all other cases the maximum deviation of duplicate determinations from their mean was 3.27%.

For reactions with rate constants larger than 10^{-2} sec.$^{-1}$ the measurements were made using the direct injection technique devised for this study. Table XIII (also, see Appendix I, Table XV) shows the results of duplicate determinations of pseudo-first-order rate constants for glucose and gives the percent deviation from the means of the duplicates. The maximum deviation from the mean was 2.46% and shows that the direct injection technique was capable of acceptable precision. The principal limitations of this technique are the length of time required for mixing (about 1 sec. for a 3-ml. sample) and the maximum chart speed (5 sec./division) which prevents accurate determination of rates greater than about 0.3 sec.$^{-1}$.

TABLE XIII

PRECISION OF KINETIC DETERMINATIONS

	Concn., M	Temp., °C.	k', $sec.^{-1}$	Deviation from Mean, %
Schardinger β-dextrin				
2583-89-3	0.040	20	0.000432	2.92
2583-78-1	0.040	20	0.000459	
Methyl β-D-glucopyranoside				
2583-73-1-A	0.040	20	0.000556	0.00
2583-73-1-B	0.040	20	0.000556	
1,5-Anhydro-D-glucitol				
2519-121-1-A	0.040	15	0.000367	1.94
2519-121-1-B	0.040	15	0.000353	
Glucose[a]				
2519-93-2-A	0.040	20	0.1452	1.16
2519-93-2-B	0.040	20	0.1486	

[a] Using direct injection technique.

EVALUATION OF KINETIC DATA

PSEUDO-FIRST-ORDER RATE CONSTANTS

For cerium(IV) oxidation reactions in which all reactants except cerium(IV) are present in large excess the rate expression becomes pseudo-first-order:

$$-dCe(IV)/dt = k'Ce(IV) \qquad (25)$$

where

Ce(IV) = total cerium(IV) concentration

k' = pseudo-first-order rate constant

Integration of the rate expression gives

$$Ce(IV) = Ce(IV)_o \exp(-k't) \quad (26)$$

where

$Ce(IV)_o$ = initial cerium(IV) concentration

or

$$\ln Ce(IV)/Ce(IV)_o = -k't \quad (27).$$

The pseudo-first-order rate constant, k', can be evaluated from the slope of a plot of $\ln Ce(IV)/Ce(IV)_o$ versus time. However, a computer program written by Hintz (5) was used to calculate the value of k' using a least squares regression technique. The exponential form of the integrated rate expression was used in the regression analysis because use of the logarithmic form gives unequal statistical weights to the data (larger weights are given to the lower concentrations) (103).

Since the integrated rate expression for a first-order reaction involves a ratio of concentrations, any linear function of the cerium(IV) concentration may be used in place of the concentrations. In the present work the spectrometric absorbance of the reaction solutions was used directly in the calculation of k'.

COMPLEX FORMATION CONSTANTS

Equilibrium constants for complex formation were evaluated by a spectrophotometric method and by a kinetic method. (See Introduction, Organic Oxidations and Oxidant-Reductant Complexes, for a discussion of appropriate theories.) The equilibrium constants were calculated from the slopes and intercepts of "reciprocal plots" in which slopes and intercepts were obtained by least squares linear regression analysis.

In determining equilibrium constants from reciprocal plots it is necessary to use the concentration of uncoordinated substrate in the reaction mixture. This concentration differs from the initial substrate concentration by the amount of substrate involved in the coordination complex and was calculated by a method of successive approximations. The initial substrate concentration was used to obtain a first estimate of the equilibrium constant. The substrate concentration was then corrected using the first estimate of the equilibrium constant and the following equations, based on a 1:1 substrate-cerium(IV) complex (5):

$$R = R_o - C \tag{28}$$

and

$$C = KRCe(IV)_o/(1-KR) \tag{29}$$

where

$\underline{R}$ = equilibrium substrate concentration

$\underline{R}_o$ = initial substrate concentration

$\underline{C}$ = complex concentration

$\underline{K}$ = equilibrium constant

$Ce(IV)_o$ = initial total cerium(IV) concentration

Then a second estimate of the equilibrium constant was obtained using the corrected substrate concentration and the process was repeated successively until the value of the equilibrium constant converged to a constant value.

THERMODYNAMIC FUNCTIONS OF ACTIVATION

The integrated form of the Arrhenius equation is

$$k = Zexp(-Ea/RT) \tag{30}$$

where

k = rate constant

Z = Arrhenius frequency factor

Ea = energy of activation, cal. $mole^{-1}$

R = gas constant, 1.987 cal. $mole^{-1}$ $deg.^{-1}$

T = absolute temperature, °K.

Taking logarithms of Equation (30)

$$\ln k = \ln Z - Ea/RT \tag{31}$$

so that for reactions exhibiting an Arrhenius temperature dependence, a plot of $\ln k$ versus $1/T$ is linear with slope $-Ea/R$ and intercept $\ln Z$. Activation energies and frequency factors were obtained from Arrhenius plots calculated using a least squares linear regression method. Apparent second-order rate constants, with units of liter $mole^{-1}$ $sec.^{-1}$, obtained by dividing the pseudo-first-order rate constant by reductant concentration, were used in the calculation of activation data so that the data of Hintz (5) could be compared with those of the present study.

Transition state theory gives the following equation relating the rate constant and the enthalpy and entropy of activation (104).

$$k = (k_B T/h)\exp(-\Delta H^*/RT)\exp(\Delta S^*/R) \tag{32}$$

where

k_B = Boltzmann constant, 1.3803×10^{-16} erg $deg.^{-1}$

h = Planck's constant, 6.625×10^{-27} erg sec.

ΔH^* = enthalpy of activation, cal. $mole^{-1}$

ΔS^* = entropy of activation, cal. $mole^{-1}$ $deg.^{-1}$

For reactions in solutions (104)

$$\Delta H^* = Ea - RT \tag{33}$$

so that

$$k = (ek_B T/h)\exp(-Ea/RT)\exp(S^*/R) \qquad (34).$$

Taking logarithms and inserting numerical values for k_B, h, and e, the base of Naperian logarithms, gives

$$\ln k = \ln T - Ea/RT - \Delta S^*/R - 24.76 \qquad (35).$$

Substituting the Arrhenius expression, Equation (31), for $\ln k$ and rearranging gives

$$\Delta S^* = R\ln(Z/T) - 49.2 \qquad (36).$$

The entropies of activation were calculated from this equation using the values of the frequency factor, Z, obtained from the Arrhenius plots.

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APPENDIX I

RESULTS OF KINETIC EXPERIMENTS

This appendix contains the results of kinetic and product analysis experiments. The original data for kinetic experiments, time and absorbance values, are given for typical reactions of four reductants. The remainder of the kinetic experiments are summarized by presenting the experimental conditions and derived rate constants. Kinetic experiments are identified by numbers which refer to The Institute of Paper Chemistry Research Notebook number, page and run number.

TABLE XIV

REACTIONS OF METHYL β-D-GLUCOPYRANOSIDE WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Substrate Concn., M	Temp., °C.	$\underline{k}'$, $sec.^{-1}$	$A_o - A_b$	Deviation from Mean, $\underline{k}'$, %
2583-74-2-A	0.080	20	0.000977	0.684	0.41
2583-74-2-B	0.080	20	0.000969	0.675	
2583-76-2-A	0.060	20	0.000704	0.579	1.54
2583-76-2-B	0.060	20	0.000726	0.564	
2583-73-1-A	0.040	20	0.000556	0.453	0.00
2583-73-1-B	0.040	20	0.000556	0.446	
2583-75-2-A	0.030	20	0.000381	0.355	0.26
2583-75-2-B	0.030	20	0.000383	0.355	
2583-73-2-A	0.020	20	0.000316	0.158	3.27
2583-73-2-B	0.020	20	0.000296	0.200	

TABLE XV

REACTIONS OF GLUCOSE WITH 0.00196M CERIUM(IV)
IN 1.0M PERCHLORIC ACID

Experiment No.	Substrate Concn., M	Temp., °C.	k', $sec.^{-1}$	Deviation from Mean, k', %
2519-93-2-A	0.040	20	0.1452	1.16
2519-93-2-B	0.040	20	0.1486	1.16
2519-93-3-A	0.040	15	0.0867	1.40
2519-93-3-B	0.040	15	0.0843	1.40
2519-122-3-A	0.040	10	0.0642	0.00
2519-122-3-B	0.040	10	0.0642	0.00
2519-103-2-A	0.030	20	0.1281	2.46
2519-103-2-C	0.030	20	0.1218	2.46
2519-104-3-A	0.020	20	0.1007	1.10
2519-104-3-B	0.020	20	0.0986	1.10
2519-104-1-A	0.015	20	0.0856	1.06
2519-104-1-B	0.015	20	0.0839	1.06
2519-105-2-A	0.010	20	0.0674	1.20
2519-105-2-B	0.010	20	0.0658	1.20

TABLE XVI

REACTIONS OF GLUCOSE WITH 0.00392M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Substrate Concn., M	Temp., °C.	k', $sec.^{-1}$	Deviation from Mean, k', %
2519-92-2-A	0.040	20	0.1426	1.11
2519-92-2-B	0.040	20	0.1458	1.11
2519-102-2-A	0.030	20	0.1307	2.67
2519-102-2-B	0.030	20	0.1239	2.67
2519-92-3	0.020	20	0.1024	1.16
2519-92-3	0.020	20	0.1048	1.16
2519-103-1-A	0.015	20	0.0819	1.45
2519-103-1-B	0.015	20	0.0842	1.45
2519-93-1-A	0.010	20	0.0644	1.07
2519-93-1-B	0.010	20	0.0658	1.07

TABLE XVII

REACTIONS OF 1,5-ANHYDRO-D-GLUCITOL WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Substrate Concn., M	Temp., °C.	k', $sec.^{-1}$	$A_o - A_b$
2519-87-1	0.080	20	0.001025	0.874
2519-88-1	0.040	20	0.000664	0.598
2519-90-2	0.030	20	0.000556	0.472
2519-90-1	0.020	20	0.000407	0.371
2519-121-1-A	0.040	15	0.000367	
2519-121-1-B	0.040	15	0.000353	
2519-123-2	0.040	10	0.000227	

TABLE XVIII

REACTIONS OF SCHARDINGER β-DEXTRIN (ANHYDRO-D-GLUCOSE) WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Substrate Concn., M	Temp., °C.	k', $sec.^{-1}$	$A_o - A_b$
2583-88-1	0.100	20	0.000837	0.654
2583-90-1	0.080	20	0.000736	0.478
2583-89-1	0.060	20	0.000589	0.453
2583-89-2	0.050	20	0.000496	0.400
2583-89-3	0.040	20	0.000417	0.318
2583-78-1	0.040	20	0.000435	0.341
2583-78-2	0.030	20	0.000353	0.294
2583-78-3	0.020	20	0.000250	0.205
2583-79-1	0.015	20	0.000207	0.147
2519-89-1	0.040[a]	20	0.000406	--
2519-122-2-A	0.040[a]	15	0.000236	--
2519-122-2-B	0.040[a]	15	0.000236	--
2519-123-1-A	0.040[a]	10	0.000188	--
2519-123-1-B	0.040[a]	10	0.000153	--

[a]Substrate concentration approximately 0.040M for these experiments. Substrate concentration constant within these experiments.

TABLE XIX

REACTIONS OF VARIOUS COMPOUNDS WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Compound (Experiment No.)	Substrate Concn., M	Temp., °C.	k', $sec.^{-1}$
Galactose			
(2519-128-1-A)	0.040	15	0.1737
(2519-128-1-B)	0.040	15	0.1760
2-O-methyl-galactose			
(2519-129-1-A)	0.040	15	0.3148
(2519-129-1-B)	0.040	15	0.3320
Methyl β-galactoside			
(2583-81-2)	0.040	20	0.001100
2-O-methyl-glucose			
(2583-94-1)	0.040	20	0.6107
2-O-methyl-glucose			
(2583-94-2)	0.040	15	0.4311
2-deoxy-glucose			
(2519-119-2-A)	0.040	15	0.003240
(2519-119-2-B)	0.040	15	0.002648
Cellobiose			
(2583-95-2)	0.040	20	0.08157
Cellobiose			
(2583-95-1)	0.040	15	0.05006
Cellobiose			
(2583-95-3)	0.020	20	0.06079
Ribose			
(2519-130-1-A)	0.040	15	0.1747
(2519-130-1-B)	0.040	15	0.1586
2,3,4,6-tetra-O-methyl-D-glucose			
(2519-82-1)	0.040	20	0.454
(2519-82-2)	0.020	20	0.223
(2519-82-3)	0.010	20	0.127
(2519-82-4)	0.005	20	0.061
Methyl-4,6-di-O-methyl-β-D-glucopyranoside			
(2457-44-2)	0.040	15	0.000164

TABLE XIX (Continued)

REACTIONS OF VARIOUS COMPOUNDS WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Compound (Experiment No.)	Substrate Concn., M	Temp., °C.	k', $sec.^{-1}$
Methyl-2,3,4,6-tetra-O-methyl-β-D-glucopyranoside			
(2457-44-3)	0.040	15	0.00001128
Glucose[a]			
(2519-66-1)	0.005	20	0.000026
(2519-66-3)	0.010	20	0.000048
(2519-75)	0.040	20	0.000165
(2519-53-1)	0.080	20	0.000340
(2519-53-2)	0.120	20	0.000499
Galactose[a]			
(2519-49)	0.040	20	0.000454
(2519-51-1)	0.040	20	0.000453
2-O-methyl-D-galactose[a]			
(2519-51-2)	0.040	20	0.000609

[a] Reactions run in mixed 0.25M sulfuric and 0.75M perchloric acids.

TABLE XX

TEMPERATURE DEPENDENCE OF REACTIONS OF GLUCOSE WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Reductant Concn., M	Temp., °C.	k', $min.^{-1}$	k'/Reductant Concn., $min.^{-1}$ M^{-1}
2519-122-3-A	0.040	10	3.853	96.25
2519-122-3-B	0.040	10	3.850	96.32
2519-93-3-A	0.040	15	5.200	130.00
2519-93-3-B	0.040	15	5.055	126.38
2519-93-2-A	0.040	20	8.713	223.02
2519-93-2-B	0.040	20	8.921	217.83

TABLE XXI

TEMPERATURE DEPENDENCE OF REACTIONS OF ANHYDRO-D-GLUCOSE (SCHARDINGER β-DEXTRIN) WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Reductant Concn., M	Temp., °C.	k', $min.^{-1}$	k'/Reductant Concn., $min.^{-1}$ M^{-1}
2519-123-1-A	0.040	10	0.01128	0.282
2519-123-1-B	0.040	10	0.0092	0.230
2519-122-2-A	0.040	15	0.01417	0.354
2519-122-2-B	0.040	15	0.01413	0.353
2519-89-1	0.040	20	0.02433	0.608

TABLE XXII

TEMPERATURE DEPENDENCE OF REACTIONS OF 1,5-ANHYDRO-D-GLUCITOL WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Reductant Concn., M	Temp., °C.	k', $min.^{-1}$	k'/Reductant Concn., $min.^{-1}$ M^{-1}
2519-123-2	0.040	10	0.01387	0.347
2519-121-1-A	0.040	15	0.02202	0.551
2519-121-1-B	0.040	15	0.02120	0.530
2519-85-1	0.040	20	0.03981	0.995

TABLE XXIII

TEMPERATURE DEPENDENCE OF REACTIONS OF METHYL β-D-GLUCOPYRANOSIDE WITH 0.00196M CERIUM(IV) IN 1.0M PERCHLORIC ACID

Experiment No.	Reductant Concn., M	Temp., °C.	k', $min.^{-1}$	k'/Reductant Concn., $min.^{-1}$ M^{-1}
2519-135-2	0.040	10	0.00857	0.214
2519-135-1	0.040	15	0.01425	0.356
2519-134-1-A	0.040	20	0.02793	0.698
2519-134-1-B	0.040	20	0.02753	0.698

APPENDIX II

TYPICAL KINETIC EXPERIMENTS

TABLE XXIV

REACTIONS OF 0.040M GLUCOSE IN 1.0M PERCHLORIC ACID AT 20°C.[a]

t, sec.	A	ln(A/A$_o$)	t, sec.	A	ln(A/A$_o$)
5	0.255	-0.725	5	0.230	-0.740
10	0.123	-1.454	10	0.106	-1.515
15	0.060	-2.172	15	0.055	-2.171
A$_o$ = 0.526			A$_o$ = 0.482		

[a] Experiment numbers 2519-93-2-A and 2519-93-2-B. Data plotted in Fig. 3.

TABLE XXV

REACTION OF 0.040M ANHYDRO-D-GLUCOSE UNITS (SCHARDINGER β-DEXTRIN) IN 1.0M PERCHLORIC ACID AT 20°C.[a]

t, sec.	A	ln(A/A$_o$)	t, sec.	A	ln(A/A$_o$)
100	0.670	-0.050	1600	0.361	-0.668
200	0.636	-0.102	1700	0.347	-0.708
300	0.612	-0.141	1800	0.330	-0.758
400	0.588	-0.181	1900	0.314	-0.808
500	0.563	-0.224	2000	0.299	-0.857
600	0.544	-0.258	2100	0.286	-0.901
700	0.521	-0.302	2200	0.270	-0.959
800	0.502	-0.339	2300	0.256	-0.012
900	0.483	-0.377	2400	0.245	-0.056
1000	0.464	-0.417	2500	0.231	-0.115
1100	0.446	-0.457	2600	0.220	-0.164
1200	0.429	-0.496	2700	0.207	-0.225
1300	0.411	-0.539	2800	0.195	-0.284
1400	0.394	-0.581	2900	0.184	-0.342
1500	0.378	-0.622			

[a]Experiment number 2519-89-3. A$_o$ = 0.704. Data plotted in Fig. 4.

TABLE XXVI

REACTION OF 1,5-ANHYDRO-D-GLUCITOL IN 1.0M PERCHLORIC ACID AT 20°C.[a]

t, sec.	A	ln(A/A$_o$)	t, sec.	A	ln(A/A$_o$)
100	0.672	-0.069	1100	0.349	-0.724
200	0.630	-0.133	1200	0.325	-0.795
300	0.590	-0.199	1300	0.304	-0.862
400	0.552	-0.266	1400	0.285	-0.927
500	0.517	-0.331	1500	0.267	-0.992
600	0.486	-0.393	1600	0.248	-0.066
700	0.453	-0.463	1700	0.232	-0.132
800	0.424	-0.529	1800	0.217	-0.199
900	0.399	-0.590	1900	0.202	-0.271
1000	0.373	-0.658	2000	0.188	-0.343

[a]Experiment number 2519-88-1. A$_o$ = 0.720. Data plotted in Fig. 5.

TABLE XXVII

REACTION OF 0.040M METHYL β-D-GLUCOPYRANOSIDE IN 1.0M PERCHLORIC ACID AT 20°C.[a]

t, sec.	A	ln(A/A$_o$)	t, sec.	A	ln(A/A$_o$)
100	0.560	-0.021	1900	0.199	-1.055
200	0.518	-0.099	2000	0.188	-1.112
300	0.487	-0.160	2100	0.179	-1.161
400	0.458	-0.222	2200	0.170	-1.213
500	0.430	-0.285	2300	0.161	-1.267
600	0.406	-0.342	2400	0.153	-1.318
700	0.380	-0.408	2500	0.145	-1.372
800	0.359	-0.465	2600	0.138	-1.421
900	0.340	-0.520	2700	0.131	-1.473
1000	0.320	-0.580	2800	0.125	-1.520
1100	0.303	-0.635	2900	0.118	-1.578
1200	0.290	-0.679	3000	0.113	-1.621
1300	0.272	-0.743	3100	0.108	-1.666
1400	0.257	-0.799	3200	0.101	-1.733
1500	0.243	-0.855	3300	0.097	-1.774
1600	0.232	-0.902	3400	0.091	-1.838
1700	0.220	-0.955	3500	0.086	-1.894
1800	0.208	-0.011	3600	0.082	-1.942

[a] Experiment number 2583-73-1-A. A_o = 0.571. Data plotted in Fig. 6.

APPENDIX III

PRODUCT ANALYSIS EXPERIMENTS

TABLE XXVIII

QUANTITATIVE DETERMINATION[a] OF GLUCOSE AND ARABINOSE IN REACTION SOLUTION FROM CERIUM(IV) OXIDATION OF GLUCOSE[b]

Compound	Analysis, mg./ml.			Weight Basis[c], %
	Test 1	Test 2	Av.	
Glucose	1.394	1.369	1.38	76.67
Arabinose	0.422	0.428	0.42	23.33

[a]The Institute of Paper Chemistry, File No. 66-72269, Appleton, Wisconsin.

[b]Oxidation conducted with 5.55×10^{-3} moles glucose and 2.775×10^{-3} moles cerium(IV) in 75 ml. 1.0M perchloric acid at 20°C.

[c]Calculation of yield based on total mass of carbohydrate (glucose + arabinose) in an aliquot of reaction solution.

TABLE XXIX

QUANTITATIVE DETERMINATION[a] OF HEXOSE[b] AND ERYTHROSE IN HYDROLYZATE OF CERIUM(IV) OXIDIZED CELLULOSE

Compound	Cerium(IV)[c] Consumed, moles x 10^5		Amount Sugar, moles x 10^5		Amount Sugar, g. x 10^5		Total Sugar[d], %	
	1	2	1	2	1	2	1	2
Hexose	239.14	262.41	19.76	21.72	3556	3802	92.8	92.6
Erythrose	18.10	20.30	2.30	2.54	276	303	7.2	7.4

[a]Method given in Reference (68).

[b]Hexose equals sum of glucose + fructose.

[c]Includes correction for consumption by impurities eluted from chromatography paper. This correction made by determining cerium(IV) consumption of eluate from blank chromatography paper (Whatman 3MM).

[d]Percent total sugar calculated on weight basis.

APPENDIX IV

THERMODYNAMICS OF ACTIVATION

The mechanism of cerium(IV) oxidations of α-glycols in 1.0M perchloric acid may be summarized as follows:

$$A + B \underset{}{\overset{K}{\rightleftharpoons}} C \xrightarrow{k} D$$

As described in the Introduction, there are methods for calculating the values of the equilibrium constant, K, and the disproportionation rate constant, k, from the kinetically determined pseudo-first-order rate constant for the overall reaction. It has been shown (p. 62) that the values of activation enthalpy and entropy determined from Arrhenius calculations based on the pseudo-first-order rate constants are actually the sums of enthalpy and entropy of both the equilibrium and rate-controlling steps.

From p. 62

$$kK = (k_B T/h)\exp[-(\Delta H + \Delta H^*)/RT]\exp[(\Delta S + \Delta S^*)/R]$$

where kK the overall rate constant as estimated by the pseudo-first-order rate constant, k', for the reaction.

$$k' = (k_B T/h)\exp[-(\Delta H^{\ddagger})/RT]\exp[(\Delta S^{\ddagger})/R]$$

then

$$\Delta H^{\ddagger} = \Delta H + \Delta H^*$$

and

$$\Delta S^{\ddagger} = \Delta S + \Delta S^*$$

where

$\Delta H^{\ddagger}$ = apparent overall activation enthalpy

$\Delta S^{\ddagger}$ = apparent overall activation entropy

ΔH = enthalpy of equilibrium step

$\Delta\underline{S}$ = entropy of equilibrium step
$\Delta\underline{H}^*$ = activation enthalpy for disproportionation
$\Delta\underline{S}^*$ = activation entropy for disproportionation

since $\Delta\underline{H}^{\ddagger}$ and $\Delta\underline{S}^{\ddagger}$ can be determined from the temperature dependence of the pseudo-first-order rate constant and $\Delta\underline{H}^*$ and $\Delta\underline{S}^*$ can be determined from the temperature dependence of the disproportionation rate constant, $\underline{k}$, then $\Delta\underline{H}$ and $\Delta\underline{S}$ can be calculated using

$$\Delta H = \Delta H^{\ddagger} - \Delta H^*$$

$$\Delta S = \Delta S^{\ddagger} - \Delta S^*$$

In order to obtain the temperature dependence of the disproportionation rate constant, kinetic experiments at several substrate concentrations are required at each temperature studied.

The data obtained in this thesis permit calculation of free energies of activation for the equilibrium step, for the disproportionation step, and for the overall reaction.

$$\Delta F^* = \Delta F + \Delta F^{\ddagger}$$

where

$\Delta\underline{F}^{\ddagger}$ = overall change in free energy
$\Delta\underline{F}$ = change in free energy of equilibrium step
$\Delta\underline{F}^*$ = change in free energy for disproportionation

$\Delta F = -RT\ln K$
$\Delta F^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$

The values of the calculated free energies are given in Table XXX.

TABLE XXX

VALUES OF CALCULATED FREE ENERGIES

	ΔF^{*}, kcal. mole^{-1}	ΔF, kcal. mole^{-1}	ΔF^{*}, kcal. mole^{-1}
Glucose	16.4	-2.1	14.3
Schardinger β-dextrin	19.8	-1.3	18.5
Methyl β-D-glucopyranoside	19.7	-1.1	18.6
1,5-Anhydro-D-glucitol	19.4	-1.5	17.9

The data available in this study do not permit calculation of the entropies and enthalpies of the equilibrium and disproportionation steps, since only one of the three unknowns can be determined. It is hoped that this discussion will permit future workers to obtain pertinent data that will enable determination of all thermodynamic activation functions.